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Original Communications

ON THE CHEMISTRY OF OVARIAN CYSTS*

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THIS report is a part of a general study on ovarian tumors. Previous reports[1-3] have been concerned with an attempt to correlate the histology of ovarian cysts, particularly that of the lining of the cyst wall, with the hormonal content of the cyst fluid. The present investigation was designed as a similar study of the chemistry of ovarian cyst fluids. It is believed that the study of the chemistry of fluids offers a unique opportunity to study the chemistry of tumors. Since most ovarian tumors are cystic, it is possible to study the chemical constituents of the fluid which is (or is not) in equilibrium with the cells of a definite and specific character which line the cyst cavity or with the fluid which results from their secretion. This is in contrast with the situation existing in a study of the chemistry of solid tumors in which the chemistry is dependent upon the proportions of different types of cells constituting the tumor tissue. Furthermore, in multilocular malignant tumors frequently only certain cyst cavities manifest malignant characteristics. In this type of tumor a parallel study of the fluids from the different cavities might offer an opportunity to observe any chemical difference between the metabolism of benign and malignant cells.

*This work has been done under a grant from the Douglas Smith Foundation for Medical Research of the University of Chicago.

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Since the physical and chemical properties of the fluids vary with the type of cyst, it is believed that a study of the chemistry of the fluids might be of value in the classification of the tumors and in the determination of the conditions governing their development and growth. A study of the electrolyte balance would throw some light on the laws governing the equilibrium between the tumor tissue and the fluid of the cyst. The part played by the secretory activity of the cells lining the cyst cavity might be shown by a study of the protein and carbohydrate constituents, particularly in those types of cysts producing unusual glycoproteins (e.g., "pseudomucin"). Since these glycoproteins occur only rarely in other body fluids they may be of special import in the metabolism of these tumors.

Although work on the chemistry of ovarian cyst fluids is of long standing and dates back to the work of Scherer[4] on protein constituents reported in 1852, comparatively little has been done using modern techniques. The early investigations were concerned chiefly with the protein constituents, especially the glycoproteins ("pseudomucins"), and with specific gravity and the percentage of solids. Surveys of the field have been reported briefly by Pfannenstiel,[5] Wells,[6] and Stolfi[7] and with a few exceptions are essentially complete. Schepetinsky and Kafitin[8] have determined calcium, potassium, sodium, phosphorus, and chloride, and observed certain deviations in the mineral content which they have attempted to correlate with the type of the tumor. Schalyt[9] found that the salt content of the fluid of neoplastic cysts was greater than that of the serum of these patients and that the reducing substance was low or absent. Schalyt[9] concluded that the development of the cyst was dependent upon two factors: namely, the secretory activity of the epithelium and the disturbance in the osmotic equilibrium. Blair-Bell and Datnow[10] have reported qualitative and quantitative data on total solid, water, inorganic matter, total nitrogen, protein, mucin, pseudomucin, cholesterol, sugar, urea, fats, fatty acids and soap. Numerous workers have reported on cholesterol and lipids in ovarian tumors but these have usually been solid tumors.

Our data have been collected in a preliminary study prior to an investigation of the glycoproteins and a study of the membrane equilibrium. Since the work has been discontinued the findings reported here are of necessity of a fragmentary nature. The data include determinations of specific gravity, solid, water, ash, sodium, potassium, chloride, total nitrogen, nonprotein nitrogen, protein and glucose. Sixteen fluids were obtained from benign ovarian cysts, twelve from malignant cysts and one from a tuboovarian cyst. Fluids from three parovarian cysts were examined also.

Description of the Pathologic Material

A specimen of the cyst wall was taken from each cavity from which fluid was obtained for chemical analysis. The various cyst cavities of

the same tumor are designated by different letters. Bilateral tumors appear with brackets in Table I with the exception of the tubo-ovarian cyst No. 343 and parovarian cyst No. 344 which also occurred in the same patient. The tissues were fixed in formalin and stained with hematoxylin and eosin.

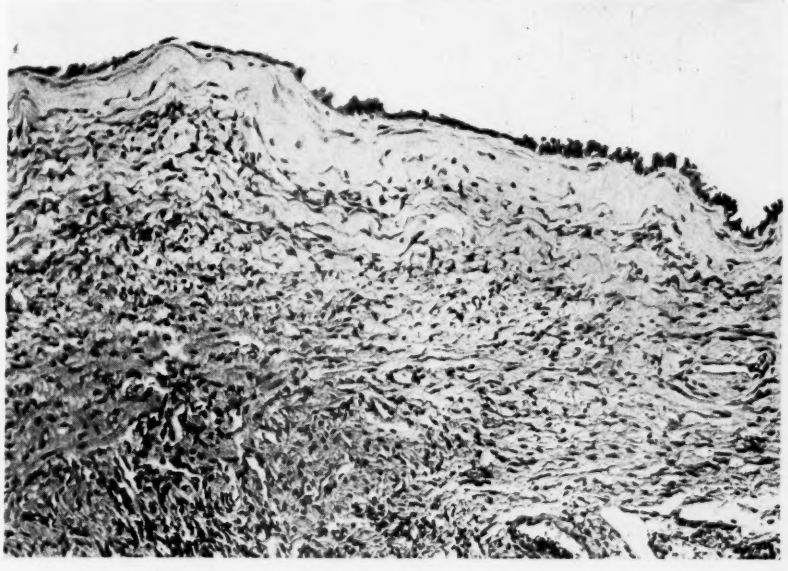

Fig. 1.—Cyst No. 341. Simple serous cyst. Low magnification (×120) showing cyst wall with irregular lining of low cuboidal epithelial cells and an underlying layer which is relatively avascular and hyalinized.

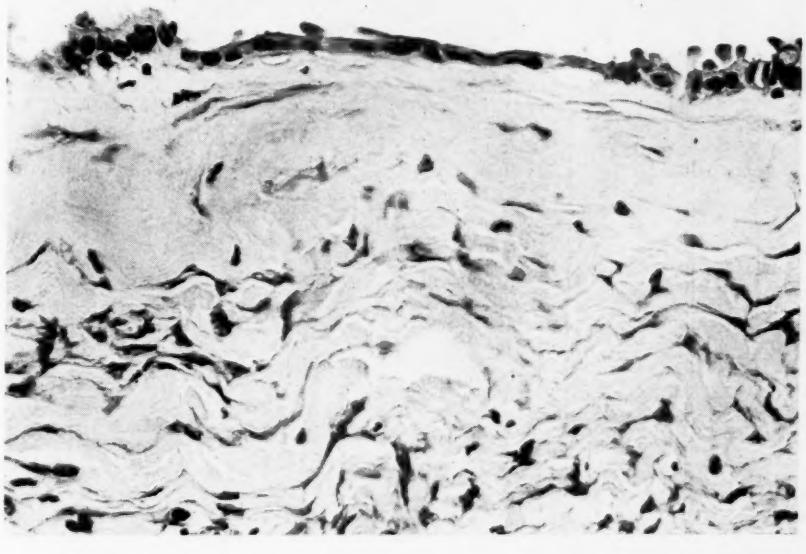

Fig. 2.—Cyst No. 341. Simple serous cyst. High magnification (×370) from section shown in Fig. 1, showing irregular epithelium and noncellular basal layer. Fluid is low in protein and potassium and high in chloride.

TABLE I. CHEMICAL COMPOSITION OF OVARIAN AND PAROVARIAN CYST FLUIDS

CYST NO.	TYPE	VOLUME FLUID ML.	% TOTAL SOLID	% WATER	% ASH	SPECIFIC GRAVITY	MG. PER L. MILLIEQUIVALENTS PER LITER				GRAMS PER LITER			
							GLUCOSE	SODIUM	POTASSIUM	CHLORIDE	TOTAL NITROGEN	NON-PROTEIN NITROGEN	PROTEIN NITROGEN	PROTEIN
						BENIGN OVARIAN CYSTS								
341	Simple serous	375	1.31	98.69	1.26	1.009		139.9	2.82	148.6	1.34	0.15	1.19	7.4
356	Simple serous	1110	0.97	99.03	1.27	1.005	30	152.2	3.16	132.4	1.76	0.12	1.64	10.3
337A	Pseudomucinous	162	15.48	84.52	1.13	1.044		153.2	5.17	87.5	21.35	0.40	20.95	130.9
337B	Pseudomucinous	268	10.98	89.02	1.18	1.034		110.2	4.30	100.7	19.63	0.54	19.09	119.4
337C	Pseudomucinous	44.5									11.61			
337D	Pseudomucinous	33						135.7	5.04	99.1	14.71			
337E	Pseudomucinous	48	17.65	82.35	1.22	1.051		127.6	5.24	92.8	23.36			
340	Pseudomucinous	1192	1.67	98.33	1.30	1.007		146.0	4.23	148.1	0.85	0.24	0.61	3.8
352	Pseudomucinous	4259	7.42	92.58	0.87		1060			136.4	3.45	0.51	2.94	18.4
358	Pseudomucinous	630	1.80	98.20	1.25	1.006	80	137.1	3.33	143.1	1.09	0.05	1.04	6.5
339A	Granulosa†	745						137.1		109.5	8.14	0.21	7.93	49.6
339B	Granulosa	415	6.32	93.68	1.18	1.019		128.8	3.05	101.9	7.53	0.21	7.32	45.8
339C	Granulosa	45	5.70	94.30	1.27	1.018		152.4		111.6	7.23	0.19	7.04	44.0
339E	Granulosa	85	5.85	94.15	1.20	1.018		138.0		114.7	6.99	0.22	6.77	42.3
339F	Granulosa	129	6.70	93.30	1.20	1.019		139.8		112.4	7.46	0.23	7.23	45.2
349	Fibro-adenoma	338	5.98	94.02	1.24	1.019	270	141.5	3.46	112.9	6.47	0.37	6.10	38.1
343*	Tuboovarian	50	1.56	98.44	1.64		11	155.1	3.88	131.4	0.49	0.11	0.38	2.4

MALIGNANT OVARIAN CYSTOMAS													
338A	5750	6.92	93.08	1.18						7.55	0.80	6.75	42.3
338B	9	11.56	88.44	0.97			131.8		100.7				
338C	8	11.42	88.58	1.16									
338D	8	7.57	92.43	1.07			117.3		95.0	12.50			
345A	431	6.88	93.12	1.18	1.020	250	135.6	4.53	117.3	9.04	0.22	8.82	55.1
345B	348	7.35	92.65	1.20	1.021	340	135.0	4.15	117.4	6.90	0.06	6.84	42.8
345C	166	4.86	95.14	1.25	1.015	340	135.6		109.1	5.69	0.15	5.54	34.6
345D	199	7.61	92.39	1.19	1.022	140	135.7	4.48	109.5	9.78	0.12	9.66	60.4
346A	141	6.64	93.36	1.20	1.020	90	141.0	5.41	115.3	8.24	0.19	8.05	50.4
351	190	8.71	91.29	0.53	1.024	90	119.3	3.09	107.1	2.19	0.35	1.84	11.5
353	15					580	135.5	3.78	109.3	13.60			
354A	79.5	8.95	91.05	1.14	1.024	60	133.9		110.6	4.06	0.37	3.69	23.1
PAROVARIAN CYSTS													
344*	88	1.58	98.42	1.58	1.006	35	134.3	3.27	127.5	0.92	0.16	0.76	4.8
348	1537	1.00	99.00	1.24	1.004	140	141.3	2.64	127.5	0.26	0.13	0.13	0.8
350	782	1.02	98.98	0.92	1.004	160	133.5	3.65	126.5	0.21	0.10	0.11	0.7

*Cysts 443 and 444 occurred in the same patient.
Braces denote bilateral tumors.
†Fluids except from locule B had a trace of blood.

The series consists of 2 simple serous cysts, 4 pseudomucinous cysts, 1 granulosa-cell tumor associated with an arrhenoblastoma, 1 cystic fibro-adenoma, 2 bilateral malignant and 2 unilateral malignant cystomas, 3 parovarian cysts and 1 tuboovarian cyst.

Brief descriptions of the microscopic findings are listed as they appear in Table I.

Cyst No. 341.—Simple serous cyst. (Figs. 1 and 2.) The lining of the cyst cavity consists of an irregular layer of low, cuboidal epithelial cells with little cytoplasm and shows evidence of degeneration. The layer underlying the lining is relatively avascular and hyalinized connective tissue.

Cyst No. 356.—Simple serous cyst. The cyst cavity is lined with single layer of low cuboidal epithelial cells consisting chiefly of chromatin and apparently not functionally active. The underlying layer is composed mostly of fibrous tissue showing some hyalinization.

Cyst No. 337.—Pseudomucinous cyst. *A.* (Figs. 3 and 4.) The lining of cyst cavity shows marked secretory activity and proliferation which is atypical in some areas and suggests malignant tendencies. The epithelial cells vary, but are mucus-containing and tall columnar in type. The wall is quite cellular and vascular and contains numerous fibroblasts.

B. The cyst wall is essentially the same as *A* but shows less papillary growth and has a slightly less dense underlying layer.

C. This cyst wall is essentially the same as *A* and *B,* but shows a more orderly arrangement and more secretory activity with numerous cells of type shown on the right of Figs. 3 and 4.

D. The cyst lining is similar to *A* but the underlying layer is composed of innumerable locules lined with regular tall columnar cells with basal nuclei. The cells are actively secreting. The fibrous tissue between the locules is quite vascular and very cellular.

E. The cyst lining is of cuboidal epithelium but the wall is denuded in most areas. Otherwise it is similar to *D* but the lining of locules is less active and more degenerate. The underlying layer is loosely fibrous and avascular but with some dense portions.

Cyst No. 340.—Pseudomucinous cyst. (Figs. 5 and 6.) The cyst is lined with a regular layer of columnar epithelial cells with basal nuclei with some tendency toward papillary growth. The cells are less actively proliferating than in Cyst No. 337. The underlying layer is not cellular; is relatively avascular, and shows some hyalinization.

Cyst No. 352.—Pseudomucinous cyst. The cyst is lined with regular layer of very tall columnar cells with basal nuclei. It is similar to Cyst No. 340 but with locules in the basal area, and slight tendency to papillary formation. The underlying layer is not cellular and is less hyalinized than Cyst No. 340.

Cyst No. 358.—Pseudomucinous cyst. The cyst is lined with high columnar cells showing secretory activity or is devoid of epithelium. The underlying layer is quite vascular and cellular in some areas but is hyalinized and not cellular in areas which are denuded.

Cyst No. 339.—Granulosa-cell tumor with probable association with an arrhenoblastoma. *A.* There is no distinct cyst wall. The cells are masses of chromatin with very little cytoplasm and the masses of cells are interspersed with fibrous tissue. The stroma is quite vascular. The underlying tissue is a fibrous layer abundantly supplied with tissue

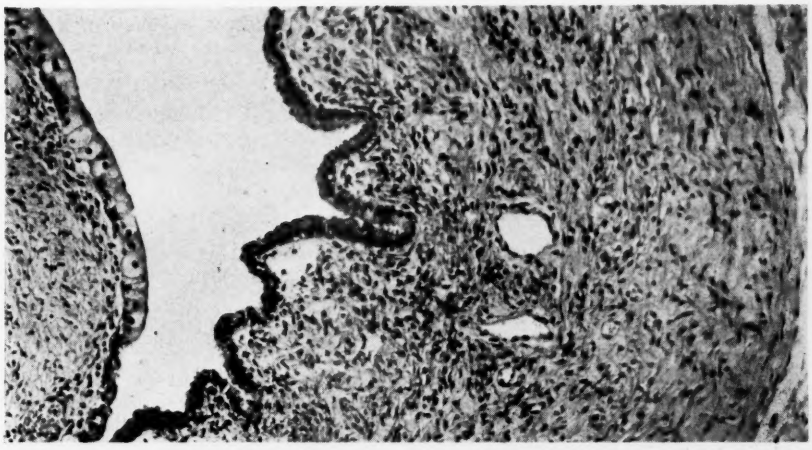

Fig. 3.—Cyst No. 337A. Pseudomucinous cyst. Low magnification (×120) of two portions of the same cyst wall showing tall columnar epithelium and cellular underlying layer.

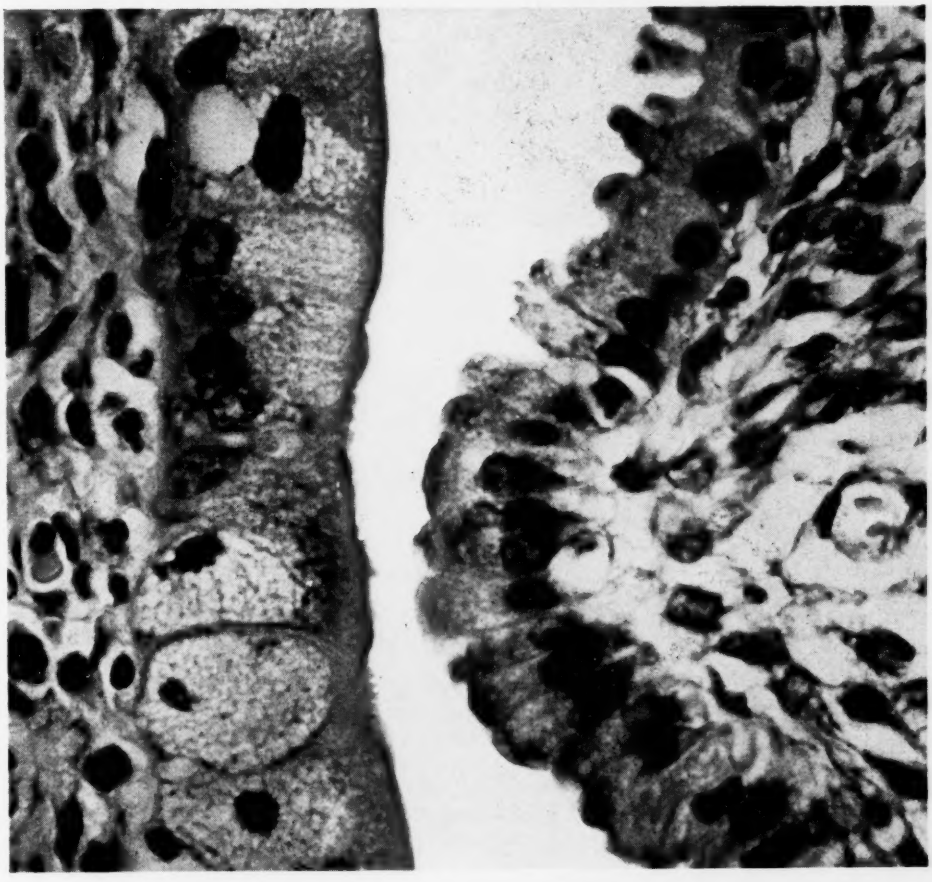

Fig. 4.—Cyst No. 337A. Pseudomucinous cyst. High magnification (×450) of two parts of same cyst wall shown in Fig. 3. Epithelial cells are actively secreting and the underlying layer is cellular. Fluid is high in protein and potassium and low in chloride.

fluids. The outer wall is fibrous and shows evidence of hyaline degeneration.

B. Same as *A.* Granulosa-cell tumor.

C. The cyst wall is thin and devoid of epithelium in most areas. The superficial layer is densely cellular, fibrous tissue underlaid with fibrous tissue with numerous blood vessels.

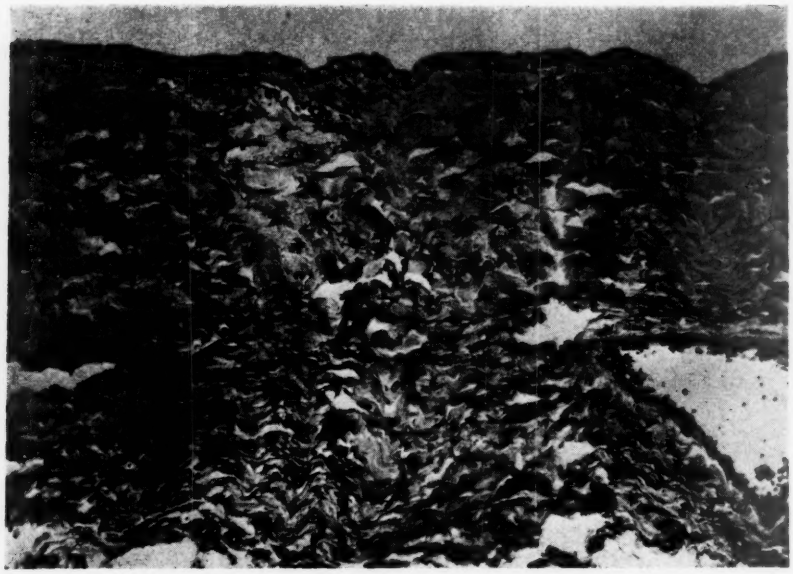

Fig. 5.—Cyst No. 340. Pseudomucinous cyst. Low magnification (×120) showing regular cyst lining of tall columnar epithelium and an underlying layer which is noncellular.

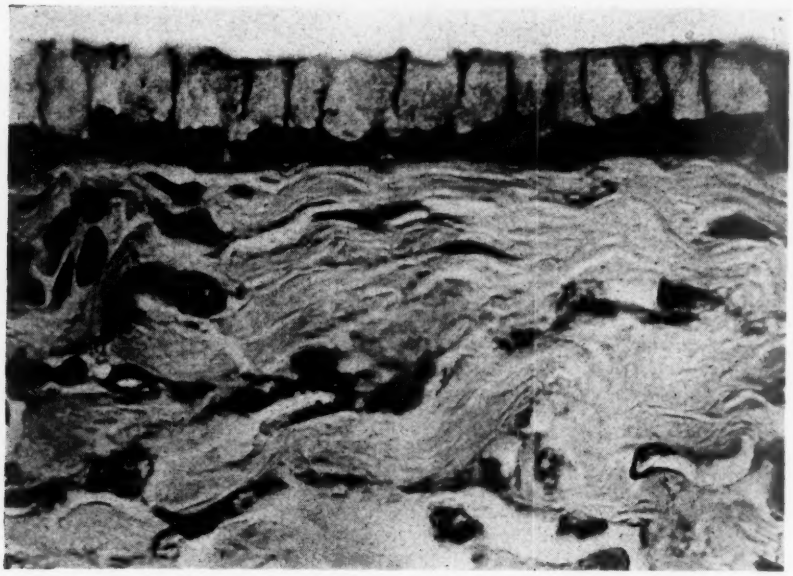

Fig. 6.—Cyst No. 340. Pseudomucinous cyst. High magnification (×450) of the cyst wall shown in Fig. 5. Cells are less actively secreting than those in Cyst No. 337A and the underlying layer is noncellular. The protein is low and the potassium and chloride are high.

E. The cyst wall is densely cellular and the microscopic section resembles those of cysts *A*, *B* and *C*.

F. This wall is devoid of epithelium and shows considerable hemorrhage and hyalinization.

Cyst No. 349.—Cystic fibro-adenoma. The cyst wall is lined by a single layer of epithelial cells which are chiefly deep-staining nuclear tissue with very little cytoplasm. In some areas the underlying tissue is cellular and in others, it is avascular and hyalinized.

Cyst No. 343.—Tuboovarian cyst. (See also Cyst No. 344 from the same patient.) The cyst wall is lined by an attenuated layer of cuboidal epithelial cells with very little cytoplasm and shows evidence of degenerative change. The underlying layer is loosely fibrous connective tissue showing hyaline changes.

Cyst No. 338.—Malignant pseudomucinous cystoma. *A*. The wall is devoid of epithelial cells except for several scattered cells. The underlying layer shows hyaline degeneration and the wall is fibrous. This section shows no evidence of malignancy.

B, *C* and *D* are sections through the area containing small locules B, C, and D. The cyst walls are lined with regular layer of tall columnar epithelium showing some functional activity. The underlying layer is not cellular, and is fibrous with a tendency toward hyalinization. There is no evidence of malignancy.

A section through the solid portion of the tumor shows the malignant character of tumor.

Cyst No. 345 and Cyst No. 346 are bilateral tumors.

Cyst No. 345.—Malignant papillary serous cystoma. *A*. The cyst is lined by irregularly proliferating low cuboidal cells which are poorly preserved and contain little cytoplasm. The underlying fibrous layer is well preserved and vascular. This is a malignant tumor.

B. The cyst is lined by atypical cells with a moderate amount of cytoplasm and shows active proliferation and papillary ingrowths. The underlying layer is cellular and the connective tissue is well preserved and reasonably vascular. This is a malignant tumor.

C. This section is similar to *B* but with glandlike structures lined by proliferating cells; some regions are lined by a single layer of epithelial cells. The underlying layer is cellular in some areas and shows hyalinization in others.

D. This cyst wall is similar to *B* with numerous papillary projections of actively proliferating atypical cells of a malignant character. The stroma is vascular and well preserved.

Cyst No. 346A.—Malignant papillary serous cystoma. This cyst wall is similar to Cyst No. 345 B and D.

Cyst No. 351.—Malignant serous cystoma. The cyst wall is devoid of epithelium in most areas, hyalinized and contains islands of adenocarcinoma cells.

Cyst No. 353 and Cyst No. 354 are bilateral malignant cystomas.

Cyst No. 353.—The epithelial lining is proliferating atypically with a tendency toward papillary growth. The connective tissue layer is fairly well preserved. The tumor is malignant.

Cyst No. 354 A.—Cyst wall is composed chiefly of proliferating cells with marked papillary growth and little stroma. The connective tissue is well preserved.

Cyst No. 344.—Parovarian cyst. (See also Cyst No. 343 occurring in the same patient.) The cyst wall is lined with a single layer of epithelial cells of cuboidal type showing some cytoplasm and slight secretory activity. There is some tendency toward papillary development with fairly normal connective tissue and vascularity but also some hyaline change. The underlying layer is not cellular.

Cyst No. 348.—Parovarian cyst. The cyst wall shows marked degeneration and is lined with epithelial cells which consist almost entirely of chromatin. The lining is lost in some areas and attenuated in others. Connective tissue is slightly vascular and shows definite hyalinization.

Cyst No. 350.—Parovarian cyst. The cyst was lined with epithelial cells which are chiefly chromatin and tend to be in more than one layer. There are some papillary tendencies. The tissue of the wall is mostly fibrous and relatively avascular.

Chemical Methods

General: The cysts were received directly from the operating room and the fluid aspirated from each cyst cavity as quickly as possible to prevent diffusion of the chemical constituents due to changes in membrane equilibrium. A specimen of tissue was taken from the wall of each cyst from which fluid was obtained for analysis. The various fluids obtained from the different locules of the same tumor are designated by different letters. Unless otherwise designated the fluids analyzed were free from blood macroscopically. Fluids were centrifuged immediately to remove any sediment. Analyses were made in duplicate or triplicate.

Specific gravity was determined at room temperature, 24 to 26° C., using calibrated 2 or 5 ml. specific gravity bottles.

Total solid and *water* were determined from weighed samples dried to constant weight at 100 to 107° C., using 2 to 5 ml. of fluid.

Ash was determined on the dried sample obtained from the total solid determination. The dried sample was ignited in a muffle furnace at 475 to 500° C., for 2 hours. It was cooled and moistened with concentrated nitric acid, heated at 475 to 500° C. for 2 hours and the ash weighed. This was repeated once or twice.

Sodium was determined by the method of Butler and Tuthill.[11]

Potassium was determined by a method based on the procedures of Shohl and Bennett[12] and Consolazio and Talbott,[13] as follows:

One milliliter of cyst fluid and 0.6 ml. 4N H_2SO_4 were heated in an oven at 100 to 107° C. in a silica crucible until charred. The crucible was placed in a cool furnace, the temperature raised gradually and maintained at 450 to 500° C., until the ash was white or nearly so. Three-tenths of a milliliter of chloroplatinic acid (10 per cent platinum) and 1 drop of 1N HCl were added to the cooled ash. After adding 5 ml. 95 per cent ethyl alcohol the crucible was placed in the refrigerator for 20 minutes. The precipitate was then transferred to a 50 ml. conical centrifuge tube by washing with portions of 95 per cent ethyl alcohol saturated with K_2PtCl_6. The precipitate was centrifuged and the washing discarded. The precipitate was triturated with 95 per cent alcohol saturated with K_2PtCl_6 and centrifuged again; this procedure was repeated. The precipitate was triturated with 10 per cent KCl solution saturated with K_2PtCl_6, centrifuged and the washing dis-

carded. The tube was placed in a water bath at 65 to 75° C., the bath raised gradually to boiling temperature and the heating continued until the precipitate was thoroughly dry and no trace of alcohol remained. Two milliliters of water were added and the tube warmed until solution was complete; 2 ml. 2N KI solution were added and the solution heated for 5 minutes and then titrated immediately with 0.01 N sodium thiosulfate.

Chloride was determined by the Van Slyke[14] method using the Wilson and Ball[15] modification.

Protein-free filtrates were obtained by the cadmium hydroxide precipitation method of Fujita and Iwatake.[16] Filtrates were made immediately. Protein was often precipitated with great difficulty from the pseudomucinous cyst fluids. It was occasionally necessary to alter the proportions of the reagents before complete precipitation was attained. Similar difficulty was observed using the tungstate method.

Total nitrogen was determined by the micro Kjeldahl method employing the Pregl technique[17] but using selenium as the catalyst. Fluids were diluted when the nitrogen value was high.

Nonprotein nitrogen was determined on the protein-free filtrate described above using the Pregl micro Kjeldahl technique.

Protein was calculated from the total nitrogen value, corrected for the nonprotein nitrogen, by multiplying by the factor 6.25.

Glucose was determined by the microtitration method of Miller and Van Slyke[18] using either the micro- or the macro-precipitation method.

Chemistry of Ovarian Cyst Fluids

The data on the chemical analyses of the cyst fluids appear in Table I. It is regrettable that there are not parallel values for the sera of these patients. Although the series is small and the data are incomplete and definite conclusions cannot be drawn, a few variations can be noted.

The *specific gravity* of the ovarian cyst fluids ranges from 1.005 for a simple serous fluid (Cyst No. 356) to 1.051 for a pseudomucinous cyst fluid (Cyst No. 337E). The values for *total solid* range from 0.97 per cent in a fluid of a simple serous cyst (Cyst No. 356) to 17.65 per cent in a pseudomucinous cyst (Cyst No. 337E). Fluids of malignant cystomas are uniformly high (4.86 to 11.56 per cent). The *water* content ranges from 82.4 per cent to 99.0 per cent. The percentage of *ash* is about 1.2 per cent, irrespective of the type of fluid or whether or not the cyst is benign or malignant. The tuboovarian cyst fluid resembled the fluid of the simple serous cysts and parovarian cysts except for a higher ash content. In general, the values are in agreement with those previously reported.

Glucose was determined by the micromethod of Miller and Van Slyke[18] in which protein-free filtrates are obtained by the method of Fujita and Iwatake[16] using cadmium hydroxide as the protein precipitant. According to Miller and Van Slyke, who confirm the work of Fujita and Iwatake, the blood filtrates do not contain more than 1.5 mg. per cent nonfermentable reducing substance. The glucose values are low compared with serum. In this respect the fluids differ from transudates. If there was any hyperglycemic effect due to anesthesia,[19] it did not affect the cyst fluids markedly. The values are in general agreement with those of Schalyt,[9] but Blair-Bell and Datnow[10] reported nega-

tive results for sugar. However, in retention cysts of the ovary, Schalyt[9] found normal glucose values but Stolfi[7] found that 3 of 8 fluids were low. Since tissue membranes are considered permeable to glucose these low values can scarcely be attributed to lack of permeability of the cyst wall. A similar situation exists in synovial fluid in which certain fluids have low glucose values. Allisson and co-workers[19] found glucose values higher in noninfected than in infected synovial fluid; Cajori and Pemberton[20] working with sterile fluids found low values when the leucocyte count was high and gave experimental evidence to support the view that the low values were due to glycolysis. Bacteriologic examinations and leucocyte counts were not made in our series but there were no evidences of inflammation. On the other hand, one might be led to consider the possible glycolytic effect of tumor tissue.

The concentrations of electrolytes vary greatly and differ from those commonly accepted for serum. *Sodium* ranges from 110.2 meq. (milliequivalents*) per liter in locule B of pseudomucinous Cyst No. 337 to 153.2 meq. in Cyst No. 337A. Seventeen of the twenty-five values (68 per cent) fall above and eight fall below the value for serum[21] (135.1 meq. per liter). A range of ±5 per cent of this value included 64 per cent of the values; 80 per cent of the values of the fluids of the malignant tumors are in this group and only 53.3 per cent of the values of the benign tumors. *Potassium* values range from 2.82 to 5.41 meq. per liter. Seventy-six and five-tenths per cent (13 of 17 values) fall below the average value for serum[21] (4.55 meq. per liter) and 64.7 per cent of the values are more than 5 per cent lower than the value for serum. *Chloride* values range from 87.5 to 148.6 meq. per liter. Seventy-three and one-tenth per cent of the values exceed the value for serum[22] (102.5 meq. per liter); 69.2 per cent exceed the value by more than 5 per cent and 42.3 per cent by more than 10 per cent. This later group includes 50 per cent of the fluids of the benign cysts and 30 per cent of those of the malignant tumors. Six of the 16 fluids of the benign tumors are more than 20 per cent above the value for serum but no fluid from a malignant tumor is above that value. The high chloride values are associated with low protein values. Schepetinsky and Kafitin[8] reported no appreciable deviation in sodium and chloride but found that the potassium values were low in fluids of serous cysts and higher in pseudomucinous cysts in comparison with the serum of these patients. Schalyt[9] reported that the salt content was higher in neoplasms than in serum but the same or slightly higher in retention cysts; Stolfi[7] noted the high salt content of retention cysts.

Total nitrogen varies extremely, from 0.49 grams per liter in tuboovarian Cyst No. 343 to 23.36 grams per liter in locule E of pseudomucinous Cyst No. 337. The fluids of the two serous cysts are very low in nitrogen but the fluids of two pseudomucinous cysts are also low. Fluids of pseudomucinous Cyst No. 337 and of two cystadenocarcinomas, Cyst No. 338D and Cyst No. 353, contain more nitrogen than serum and several others approach that value. *Nonprotein nitrogen* values vary from 0.05 to 0.80 grams per liter. Fifty per cent of the values are more than 20 per cent below and 31.8 per cent are more than 20 per cent above the average value for serum (0.28 grams per liter). These low values may be due chiefly to the use of cadmium hydroxide as the protein precipitant. *Protein* varies from 2.4 to 130.9 grams per liter.

*The use of the term "milliequivalent" in expressing electrolyte concentration is discussed in J. A. M. A. 115: 1041, 1940.

Chemistry of the Parovarian Cyst Fluids

The data on the chemical analysis of the fluids of parovarian cysts appear in Table I. The specific gravity and the total solid values are low but the values for the ash are not uniform. The low glucose values are in agreement with the findings of Dierks and Becker[23] who found low values and with Stolfi[7] who reported low values in 4 of 8 fluids, but not with the negative findings of Blair-Bell and Datnow.[10] Sodium values are about the same as for serum but the potassium content is low and the chloride concentration high. The nitrogen and protein content is much lower than in ovarian cyst fluids and the N.P.N. value is also low. In general, the values agree with those previously reported by Dierks and Becker[23] although Stolfi[7] reported N.P.N. values corresponding to those of serum. The values resemble those of simple serous cysts and other cysts which are not actively secreting.

The Relation of the Chemistry of the Cyst Fluid to the Histology of the Tumor

Not only do the fluids of different types of cysts vary in their chemical composition, but fluids of the same type or even of the different locules of the same tumor differ. In general, the chemistry of the fluid seems to be related to the secretory activity of the epithelial lining of the cyst wall and the basal underlying layer. Those cysts showing marked secretory activity or having an underlying cellular layer have fluids with high protein, low chloride and high potassium; those with less actively secreting epithelium, and showing an avascular or hyalinized basal layer, have fluids which are low in total solid and protein, high in chloride and low in potassium. Cysts in which the wall is denuded or attenuated are also of this type. Except for the higher protein content these fluids resemble transudates in type.[24] When the wall of the cyst is secretory in type, the composition of the fluid depends not only upon the osmotic equilibrium, but also upon the activity of the epithelial cells. This is a complicating factor because the electrolyte pattern, according to Donnan's equilibrium, is governed not only by the concentration of the electrolytes but also by the amounts of the nondiffusible substances, such as proteins, which are being produced by the cells of the lining.[25] The amount of protein present may depend not only upon the secretory activity of the cyst lining, but also upon the fact that the permeability of a membrane to blood proteins may be altered by a variety of circumstances. The final equilibrium will be subject to the factor of hydrostatic pressure.

That the chemistry of the cyst fluid is related to the character of the tumor is illustrated by two pseudomucinous Cysts, No. 337A and No. 340. Cyst No. 337A (Figs. 3 and 4) has a cyst cavity lined with proliferating epithelial cells with marked secretory activity; the underlying layer has numerous fibroblasts and is quite cellular and vascular. The fluid was high in protein and low in chloride. Cyst No. 340 (Figs.

5 and 6) has a regular lining of epithelial cells showing little evidence of secretory activity and essentially no tendencies toward papillary growth; the underlying layer is relatively avascular and hyalinized. In spite of the pseudomucinous type of the cyst and mucus-containing cells, the fluid is low in nitrogen and protein and high in chloride. Cyst No. 358 is similar to Cyst No. 340 but the wall shows less hyalinization and there is more activity in the cells of the lining. The chloride is lower and the protein is higher than in Cyst No. 340 but the chloride is not as low or the protein as high as in the very actively proliferating Cyst No. 337A. The cyst wall of simple serous Cyst No. 341 (Figs. 1 and 2) shows an irregular lining of low cuboidal cells with little cytoplasm but some degenerative change; the underlying layer is avascular and hyalinized. The fluid is low in protein and potassium and high in chloride. There is a close resemblance between this type of cyst and parovarian cysts both in the histology of the cyst wall and the chemistry of the cyst fluid. The fluids of parovarian cysts are also low in nitrogen and potassium and high in chloride.

Summary and Conclusions

Determinations of sodium, potassium, chloride, nitrogen, nonprotein nitrogen, protein, glucose, total solid, water, ash and specific gravity have been made on 29 ovarian cyst fluids from 15 ovarian tumors (9 benign and 6 malignant); three fluids from parovarian cysts have been examined. Values vary greatly not only among the fluids of different types of cysts, but also between the fluids of the different cavities of the same tumor. The findings are correlated with the histology of the tumor. The composition of the fluid seems to vary with the secretory activity of the lining of the cyst. In general, fluids from cysts with actively secreting epithelium and a cellular basal layer are high in nitrogen and protein, high in potassium and low in chloride; those with less actively secreting epithelium, or a cyst wall which is denuded or attenuated, and in which the basal layer is avascular or hyalinized show low nitrogen and protein, low potassium and high chloride.

We wish to express our appreciation to the members of the staff who have made the clinical material available.

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CESAREAN SECTION MORBIDITY AND SEPTIC MORTALITY IN RELATION TO THE TYPE OF OPERATION*

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PREVIOUS reviews of cesarean sections show that the death rate from this procedure drops sharply as the percentage of elective operations increases. When the operation follows a period of labor, however, there is an increase in deaths commensurate with the duration of labor. Septic infection, notably peritonitis, holds an unenviable position as chief of the causes of death following abdominal delivery, accounting for 36.3 per cent of the deaths in Philadelphia in 1941. We[1] have reported elsewhere that the Philadelphia Maternal Mortality Committee deemed preventable nearly one-third of the septic cesarean deaths occurring in the years 1931 to 1940 inclusive because the operation followed prolonged labor. The results of a questionnaire sent to Philadelphia hospitals in 1940 by Schumann[2] showed that 4.2 per cent of the sections performed in that year were of the "neglected dystocia" variety. Realizing that even now a woman dies in this city from post-cesarean sepsis every five weeks and that more than a third of the operations still are accomplished after a period of labor, in fifteen per cent of which the membranes are ruptured and prior vaginal examination performed, it would seem fitting to review this problem from the standpoint of morbidity and mortality in relation to the type of operation.

A voluminous literature discloses debates, sometimes acrimonious, concerning the merits of the various types of cesarean section. In the discussion following a report by Lull[3] on cesarean sections in Philadelphia in 1931 and 1941 respectively, it was generally agreed that there was little need for the extraperitoneal operation as advocated by Waters, Burns, Aldridge, Ricci and others. Gustafson[4] in a recent review of transverse cervical sections concludes that the extraperitoneal approach would have offered no increased protection to his patients and states that the Porro operation is the procedure of choice when actual infection exists. In their reports Fall[5] and Ryder[6] cast doubt on the superiority of the low segment operation. At the Philadelphia Lying-in Hospital there is no routine operation. A majority of the staff prefers the classical operation for the patient not in labor, reserving the Kerr cervical section for the patient in labor or with ruptured membranes and the Waters or Porro operation for the infected patient.

It is reasonable to propose that a woman can rarely die of sepsis unless the postoperative course has been morbid. To determine the current

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relationship of the type of operation to morbidity, we have reviewed all cesarean sections performed at the Philadelphia Lying-in Hospital during the past three years. The gross morbidity is expressed according to the standard of the American Committee on Maternal Welfare. During this period there have been four hundred and nine cesarean sections performed by twenty-nine operators with three deaths or 0.7 per cent. Distribution of the operations by type is shown in Table I.

TABLE I. DISTRIBUTION OF OPERATIONS BY TYPE

	NUMBER	PERCENTAGE IN LABOR
Classical	286—69.9%	10.1
Low	103—25.2%	53.3
Porro	15— 3.7%	26.6
Waters	5— 1.2%	100.0

In comparing the results of the classical and low operations we find that ninety per cent of the patients having a classical section were operated upon before labor began with a total morbidity of 25.5 per cent compared to 28.1 per cent for the low operation, 53.3 per cent of whom were in labor. Table II shows that the low section is followed by much lower morbidity except in the group in labor under twelve hours.

TABLE II. MORBIDITY IN RELATION TO THE DURATION OF LABOR

	CLASSICAL		LOW	
HOURS OF LABOR	NUMBER	% MORBID	NUMBER	% MORBID
0	256	23.3	48	12.5
0 to 12	23	30.4	24	33.3
12 to 24	4	100.0	22	45.4
24 plus	2	100.0	9	55.5
Average days morbid	3.5		4.1	

However, in this group the duration of labor in the low sections generally approached twelve hours, while most of the classical sections were performed after less than three hours of labor. It is noteworthy that six patients, all morbid, had classic operations after more than twelve hours of labor. One of these also had ruptured membranes for sixty hours, was severely infected and was hospitalized seventy-four days.

If the membranes were ruptured (Table III) the percentage of morbidity rose and again the low operation shows a more favorable rate.

TABLE III. MORBIDITY IN RELATION TO RUPTURED MEMBRANES

	CLASSICAL		LOW	
DURATION	NUMBER	% MORBID	NUMBER	% MORBID
0	275	24.0	67	19.4
0 to 12	6	33.3	21	42.7
12 plus	4	100.0	15	46.6

If labor had progressed until there was a temperature elevation, the morbidity was 60 per cent in the fifteen low sections and 100 per cent

in the five classical operations exhibiting this complication. The morbidity rate in two hundred and fifty-eight elective classical sections with unruptured membranes was 23.2 per cent in contrast to 9.5 per cent in forty-two similar low operations. On the other hand when there had been labor for twelve hours with ruptured membranes, 55 per cent of the low sections were morbid in comparison to 100 per cent of the classical. A single vaginal examination preceded the classical operation in fourteen instances while the increase was 250 per cent before the low operation, some patients having had as many as three examinations.

We have favored the use of continuous caudal and low dose, continuous spinal anesthesia in the absence of placenta previa, shock or severe anemia. A comparison (Table IV) of the morbidity rates shows a very minor improvement in elective cases but the postoperative condition of the patient and the uterine tone is vastly improved under block anesthesia.

TABLE IV. MORBIDITY IN RELATION TO ANESTHESIA
(No Labor and With Intact Membranes)

	CLASSICAL		LOW	
	NUMBER	% MORBID	NUMBER	% MORBID
Continuous spinal and Continuous caudal	67	22.3	22	9.0
General	191	23.5	20	10.0

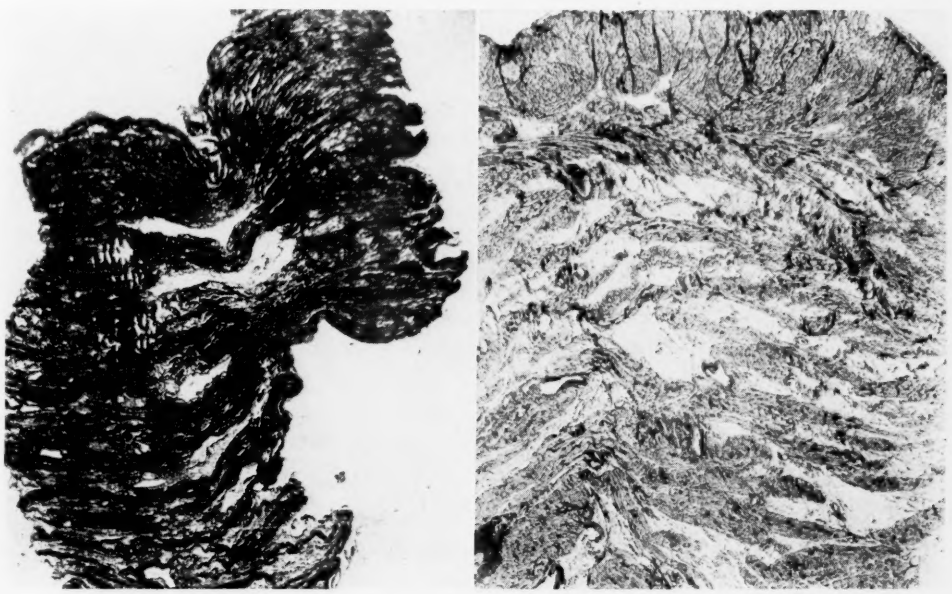
It is the opinion of the author that the former objections to spinal anesthesia do not hold if one (a) uses an initial dose not over 50 mg., (b) verifies stabilization of the blood pressure before emptying the uterus, and (c) uses only a 2.5 per cent anesthetic solution. These conditions are possible only when using the fractional method described by Lemmon.

One of the advantages of the classical operation is said to be a shorter operating time but this was not appreciable in our series. The supposed difficulty in incising and developing the bladder flap was not apparent since this procedure, in timed cases, was a matter of seconds. The shortest operation recorded was a Kerr cervical section which took exactly ten minutes. Labor is unnecessary to the performance of the low operation, since nearly half of our operations of this type were performed before labor began.

Adhesions due to a previous classical operation were found in thirty-eight instances compared to six where the previous operation had been of the low type. This incidence was twice as great as the relative proportion of operations. To prevent these adhesions Schumann advocates the development of a peritoneal flap before making a fundal incision but it would seem easier to use the peritoneal reflection already provided by nature.

Another factor not yet considered is the reported superiority of the low section in preventing subsequent rupture of the uterus. There

were three ruptured uteri following classical operations in this series, an incidence of 1 per cent. In addition, there were very thin scars in four more cases. One other rupture followed a Waters section but it occurred in the posterior wall of the fundus far removed from the scar. There were no ruptures of low scars. Elton[7] reports an incidence of rupture of 1.5 per cent following thirty-three hundred classical operations. In contrast Waters,[8] in a series of fifteen hundred sections, 70 per cent of which were of the low type, reports five ruptures following classical operations and none following the low. Grusetz and Tisdall[9] were able to report only six cases of ruptured low transverse scars in the literature despite the increased performance of this operation. The opinion that the increased use of the low section will result in an equal incidence of ruptured scars is certainly unprejudiced by past performance.



A. *B.*

Cesarean section morbidity and mortality

Fig. 1.—Photomicrograph (×20) of lower uterine segment *A*, and upper uterine segment *B*, stained for connective tissue (azocarmine). Note marked predominance of connective tissue in the lower uterine segment.

Comparable sections of the uterine wall (Fig. 1) taken from Kerr and fundal incisions when stained for connective tissue show a marked predominance of this tissue in the lower segment. In fact the lower uterine segment is covered by a real layer of fascia plainly visible at operation and well described as a continuation of the vesicovaginal fascia which thins out at Braun's ring. When closing the abdominal wall, it is upon fascia, not muscle, that one depends for strength and this likewise should apply to a uterine incision.

There were fifteen Porro operations performed, ten for uterine fibroids, three for ruptured uteri and two for uterine atony. The morbidity incidence was 13.3 per cent.

All five Waters operations were performed on patients who had been in labor over twenty-four hours, with an average duration of thirty-six hours. In every case the membranes had been ruptured prior to operation for an average of thirty hours. All the patients had one or more vaginal examinations before operation and there were preoperative temperature elevations in three instances. The morbidity incidence was 40 per cent with an average duration of three days.

If the proposition that septic death can rarely occur in an afebrile patient is valid, the morbidity figures at the Lying-in Hospital attest to the greater safety of the low operation for the patient in labor. The presence of postoperative adhesions is a decided disadvantage of the classical operation and may occasionally cause death from mechanical intestinal obstruction as reported by Manahan.[10] There would seem to be little doubt that the low transverse incision offers increased protection against subsequent rupture of the scar. The morbidity rate for the Porro operation is low but all of these operations were performed in clean cases. On the other hand three of the Waters sections were definitely infected before operation, two of them having had prior intrauterine manipulations. The remaining two were cases of serious potential infection. The absence of signs of peritoneal irritation was remarkable considering the extent of infection preoperatively.

Since the deaths from postcesarean sepsis in any one hospital are not large, it was decided to study the records of such deaths provided through the courtesy of the Maternal Mortality Committee of the Philadelphia County Medical Society. From 1931 to 1942 inclusive, one hundred and fourteen deaths from sepsis followed cesarean section. Table V shows the distribution of these deaths by type of operation.

TABLE V. TYPE OF OPERATION AND DURATION OF LABOR IN FATAL CASES

TYPE	NUMBER	HOURS OF LABOR					
		0	0 TO 12	12 TO 24	24 TO 48	48 PLUS	UNKNOWN
Classical	71	30	8	6	21	5	1
Low	20	2	2	4	9	1	2
Porro	8	3	1	1	2	1	0
Extraperitoneal	3	0	0	1	2	0	0
Unrecorded	12	4	3	2	2	1	0
Total	114	39	14	14	36	8	3

The twelve cases listed as "Unrecorded" were performed in 1931 and were undoubtedly classical in type. It will be noted that 70 per cent of the low and 100 per cent of the extraperitoneal compared to 45 per cent of the classical operations were preceded by a period of labor of twelve or more hours. In addition, the low operation was performed more often when other unfavorable conditions (Table VI) were present.

TABLE VI. ANTECEDENT FACTORS IN 114 SEPTIC DEATHS

Operation after trial of labor	65%
Duration of labor over 12 hours	50%
Duration of labor over 24 hours	38%
Ruptured membranes	36%
Preoperative temperature elevation	37%
Preoperative vaginal examination	47%

The distribution of cesarean sections in Philadelphia by type of operation in 1931 and 1941 has been reported by Lull.[3] Comparison (Table VII) of the incidence of these operations with the distribution of deaths from sepsis according to type of operation for these two years shows an advantage in favor of the low operation.

This is less apparent in 1941 than 1931, probably as a result of the general trend toward increased use of the low section when unfavorable factors are present. More marked than this, however, is the very high death rate from the Porro operation which is usually thought of as the procedure of choice in the infected case. It will also be seen (Table VIII) that in 1941 all of the women dying from sepsis following the low or Porro operation had been in labor while death from sepsis following the classical procedure was preceded by labor in only half of the cases. Again it is seen that the Porro operation results in a high septic death rate.

TABLE VII. INCIDENCE OF OPERATIONS BY TYPE COMPARED TO PERCENTAGE OF DEATHS FROM SEPSIS IN 1931 AND 1941

	1931		1941	
TYPE	INCIDENCE	DEATHS	INCIDENCE	DEATHS
Classical	79.9%	85.0%	61.5%	60.0%
Low	17.9%	5.0%	36.2%	30.0%
Porro	1.7%	10.0%	1.9%	10.0%

TABLE VIII. INCIDENCE OF DEATHS FROM SEPSIS BY TYPE OF OPERATION WITH PERCENTAGE IN LABOR IN 1931 AND 1941

	1931			1941		
TYPE	NUMBER	DEATHS	IN LABOR	NUMBER	DEATHS	IN LABOR
Classical	458	3.4%	70.5%	550	1.1%	50.0%
Low	103	0.9%	100.0%	324	0.9%	100.0%
Porro	10	20.0%	100.0%	17	5.8%	100.0%

As the advantages of the Kerr section have become appreciated, it has been performed more frequently in potentially infected patients and the relative percentage of deaths from sepsis following its use has risen but the absolute percentage remains the same. Thus it would seem that this operation is safe for the patient who has been in labor twelve to twenty-four hours with no other unfavorable factors present. But what of the small group of neglected dystocia patients from which comes the majority of our septic deaths? Should we sacrifice the uterus or will an extraperitoneal operation offer as much or more protection? Reported series[11-20] of Porro operations shows that most of these

are performed for fibroids, uterine atony, rupture or abruption and not for infection. Yet in Philadelphia the death rate from sepsis *alone* was 20 per cent in 1931, and 5.8 per cent in 1941 for all Porro operations. At the Lying-in Hospital only two Porro operations have been performed for infection during the past twelve years. One patient died of shock during the operation, the other died of peritonitis. Of the seventeen Porro operations performed in Philadelphia in 1941, only one was for infection and that patient died of peritonitis. Conversely, Waters* recently reported only two deaths from all causes in a total of two hundred and fifty extraperitoneal operations. Ninety of these were in patients septic before operation who had had more than forty-eight hours of labor. Positive cultures for pathogenic bacteria were obtained at operation in sixty instances. Irving[11] in 1937 compared the extraperitoneal with the Porro operations then recorded and showed that the latter had a 100 per cent higher mortality rate. If the remaining uterus is a focus of infection more important than peritoneal spill as a precursor to septic death, why do we fear death from peritonitis following uterine rupture where the focus is removed but peritoneal spill is not avoided. When one incises the lower uterine segment in an infected patient, that portion of the uterus most grossly contaminated is invaded and it would seem safer to confine the resultant spill to an extraperitoneal space which can be drained rather than to permit its entrance into the peritoneal cavity. At any rate, the fatal results from the

TABLE IX. MORTALITY FOLLOWING PORRO AND EXTRAPERITONEAL OPERATIONS

PORRO					EXTRAPERITONEAL		
AUTHOR	TOTAL CASES	TOTAL DEATHS	NO. FOR INFECTION	NO. DEATHS IN SEPTIC CASES	AUTHOR	NUMBER	DEATHS
Greenhill[12]	38	0	1	0	Steele[21]	59	5
Hawks[13]	11	1	2	1	Fleisher and Keeshner[11]	19	0
Lash and Cummings[14]	53	6	12	4	Hawks[13]	30	0
Adair[15]	20	0	8	0	Burns[21]	79	2
Phaneuf[16]	25	0	7	0	Cosgrove[21]	74	2
Lazard[17]	39	0	1	0	Irving[11]	23	0
Daily[25]	30	0	30	0	Sackett[11]	51	4
Maxwell[18]	11	2	2	1	Perrins[11]	22	0
Lazard[19]	51	4	9	2	Holterman[11]	194	10
Arnot[20]	10	2	10	2	Waters	90	2
Briscoe	27	5	3	3	Eisaman and Austin[22]	22	0
					Williamson and Goldblatt[23]	25	0
					Pieri and Irving[24]	20	0
					Briscoe	9	0
Total	315	20 (6.3%)	85	13 (15.2%)		717	25 (3.4%)

*Reported at a meeting of the Obstetrical Society of Philadelphia, February 3, 1944.

Porro operations performed for infection in this city compared to the results of our own and reported series[21-25] of extraperitoneal operations would prove this to be more than mere speculation.

Summary

1. Cesarean section performed before labor begins offers the patient the most protection against sepsis.

2. Postcesarean morbidity rates at the Philadelphia Lying-in Hospital during the past three years show superiority of the low section over the classical for the elective case and especially for the patient in labor.

3. Over a third of the women who die in Philadelphia following cesarean section die of sepsis.

4. One-half of these deaths occurred in patients who had been in labor over twelve hours before operation, 37 per cent of whom showed signs of sepsis preoperatively.

5. The absolute death rate and the relative death rate from sepsis show superiority of the low operation for the elective case and especially for the patient in labor.

6. The supposed protection of the Porro operation for the infected patient has been lacking in Philadelphia during the past twelve years.

7. Reported series of extraperitoneal operations shows the death rate from all causes to be from two to five times less than the death rate from sepsis alone for the Porro operations performed in this city.

8. The operation of choice for the infected patient would seem to be an extraperitoneal cesarean section.

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255 SOUTH SEVENTEENTH STREET

Discussion

DR. CLIFFORD B. LULL.—Surveys of cesarean sections which we made in 1931, and again in 1941, showed that the mortality rate depends on three factors: first, the time the operation was done; second, the type of operation performed; and third, the anesthesia that was used. Dr. Briscoe's paper brought out all of these three factors again. I still believe that there is a place in obstetrics for the low classical cesarean section. For example, the patient who has had a previous cesarean operation and is going to be sterilized at operation performed at the time of election, is a suitable case for the low classical. In doing the low segment operation, I believe that the Kerr incision is better than the longitudinal, but in certain cases where the head is unusually large, we do the longitudinal incision because it may be extended, allowing us to deliver the head more easily. As to the Porro operation, Dr. Briscoe brought out a very interesting point; namely, that women potentially infected are just as likely to die following this as after one of the other types of section, except the extraperitoneal. We have not had an opportunity to do very many of the Waters' type of section. Those that we have seen, however, were all potentially infected women who had been in labor a long time, but who made a very satisfactory convalescence. I believe it will be some time before any of us will have an opportunity of doing very many of this type as most of our cases are sectioned before they reach the point of potential infection.

DR. JOHN COOKE HIRST, II.—The topic is timely because we are still discussing the relative advantages of classical vs. low operations, and Dr. Waters has demonstrated that we did not know all there is to know about cesarean section. Also, Dr. James S. Taylor, Chairman of the Pennsylvania State Maternal Welfare Commission has been greatly concerned about poor results from cesarean sections for many years. I have a report of the first six months of 1941, where we see a total of 86,000 births and 209 maternal deaths in Pennsylvania, of which the largest cause of deaths was eclampsia with 38 cases, but 28 cesarean deaths, not counting 11 additional deaths where cesarean section was done for other reasons, which might be attributed to the operation, so that we certainly can improve our cesarean section results according to this analysis.

I am particularly interested in the subject because of experience with a type of transperitoneal exclusion low cesarean section for the frankly infected case rather than hysterectomy, namely the Pfannenstiel-Kerr-B. C. Hirst procedure, which was not done by my late father, but utilizes his exclusion principle with good results. You are familiar with a similar technique described by Dr. Erwin Smith of New York, and Dr. Frost of Morristown, N. J. There is no question that sulfonamide has imposed an obligation on us that is, rather than rely on hysterectomy, to become thoroughly comfortable in doing some type of exclusion or extraperitoneal operation, of which I think the Waters is the best. My own personal preference is, first, the Kerr operation for the elective case, then the Beck section for the doubtful patients, and the transperitoneal operation for the obviously infected patient—all of them to be done under continuous caudal or spinal anesthesia.

DR. OWEN JONES TOLAND.—There is a question that I should like to ask Dr. Briscoe, whether or not the cases that he refers to as dying of peritonitis were actually proved by autopsy to be peritonitis. In my own experience, I have found death following cesarean section to be most unusually associated with peritonitis;

the cause of death has been sepsis, yes, but the septic process has extended via the uterine wall, through lymphatics, to the parametrial tissue and to the blood stream. The peritoneal cavity has not been invaded. It is true that many of these cases have a paralytic ileus, and I have often wondered if many of the cases described in the Report of the Mortality Committee as dying of peritonitis, are not actually sepsis with paralytic ileus and without peritonitis.

DR. BRISCOE (closing).—The Kerr operation was stressed by me, first, because our morbidity statistics were compiled chiefly from this procedure. Second, it is a simple geometric fact that a curved incision affords more room for extracting the fetus. Last, the protection against subsequent rupture applies more correctly to this operation. Kletzhändler (AM. J. OBST. & GYNEC. 47: 132, 1944) reviewed the reports of 402 cases of rupture of the uterus; 196 followed fundal incisions, 87 longitudinal cervical incisions, but only 5 occurred after transverse cervical incisions. There was no information in the remaining 104 cases. The lower uterine segment is predominately connective tissue, and it is possible to place a low-curved transverse incision entirely within this area which will be strong, whereas the cervical longitudinal incision almost invariably extends up into the weaker, muscular portion of the fundus.

Sulfanilamide powder should certainly be used as suggested by Dr. Hirst. This does not always overcome the infectivity of the peritoneal spill, however, for in the first nine months of 1943, five of the seven women who died of sepsis had generalized peritonitis despite the use of this drug.

To answer Dr. Toland's question, let me state that 80 per cent of the 45 patients who were autopsied had peritonitis. It was present following the different procedures in these percentages: classical 80 per cent, Porro 100 per cent, low cervical 66.6 per cent and extraperitoneal 50 per cent.

I have an additional table showing the results of reported series of Porro and extraperitoneal operations mentioned in the paper. The mortality incidence for 315 Porro operations was 6.3 per cent. However, only 85 of these were done for actual or potential infection with a death incidence in this group of 15.2 per cent. Compared to this are 717 extraperitoneal operations with a mortality incidence of only 3.4 per cent.

Dr. Williams is correct in stating that we should have a "maternal protection society" since 4 per cent of our cesarean sections (in this city), are done in the presence of neglected dystocia. What this really means is that 40 women every year need the added protection of an extraperitoneal operation. This should remove any doubts from the minds of those who state that here in Philadelphia, there is no need for the Waters' operation at this time of enlightened practice.

ZONDEK'S SIMPLIFIED TREATMENT OF SECONDARY AMENORRHEA

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CESSATION of cyclic uterine bleeding in the nonpregnant woman of childbearing age with intact pelvic organs is sometimes a source of grave concern to the patient and her family; frequently women thus afflicted develop various neuroses and depressive states. Therefore, it is often imperative to produce uterine bleeding in order to reassure the patient and help her toward an adjustment of her problems; in many instances this should be done in the shortest possible time. Whether the uterine bleeding induced is a physiological menstruation or the result of substitution therapy is immaterial to the patient; the external manifestation of uterine bleeding suffices to reassure her that the normal function was not completely lost.

In a large number of cases amenorrhea is due to pelvic pathology, debilitating diseases, nutritional deficiencies and psychogenic disturbances. Hereditary tendencies, too, must be considered, as well as diseases and tumors of the central nervous system and of the endocrine glands. In the balance of the cases the disorder is endocrine in origin. As a matter of fact, the various types of functional amenorrhea constitute the majority of amenorrheic cases. The glands which are commonly concerned are the thyroid, the pituitary, the ovaries, and the adrenals.

Amenorrhea caused by thyroid disturbances is comparatively rare; when encountered it readily responds to treatment. Amenorrhea due to a mild pituitary or ovarian deficiency often responds to stimulative glandular therapy. However, the more severe types of amenorrhea, which are due either to adrenal overactivity or to the primary pituitary or primary ovarian deficiency rarely respond to stimulative therapy; in these instances substitution therapy with potent estrogens and progestogens is indicated.

Ever since glandular and hormonal preparations became available, the medical profession has sought earnestly for a treatment plan which is both simple and effective in inducing uterine bleeding. The commercial production of estradiol and its derivatives as well as of progesterone paved the way for further progress in this direction. Considerable advance in simplifying the heretofore commonly employed cyclic hormonal therapy of secondary amenorrhea was made by Zondek[1] who demonstrated that out of a group of 17 patients with secondary amenorrhea of from 6 months to 9 years' duration, 11 cases (64.7 per cent responded favorably to the simultaneous administration of progesterone, 12.5 mg., and of estradiol benzoate, 2.5 mg. each on two consecutive

days. Bleeding ensued 48 to 112 hours after the second injection and the majority of nonreactors were found to be those patients who had been amenorrheic for more than 2 years. Therefore in order to improve the percentage of positive results Zondek suggests that the two-day treatment plan should be restricted to cases of less than 2 years' duration.

Berlind[2] presenting 9 cases of secondary amenorrhea, employed Zondek's simplified technique in 7 patients, 3 of whom had been amenorrheic for more than two years. In these latter cases, though, bleedings induced by other hormonal measures had preceded the two-day treatment and thus the responsiveness to the condensed therapy was probably greater than was to be expected in view of the duration of the amenorrhea. For all practical purposes therefore, all of Berlind's 7 patients subjected to the two-day treatment plan, they received a total of 9 courses, may be considered as falling into the group of amenorrhea of less than 2 years' duration. In each single instance, bleeding occurred, 2 to 4 days after the second injection.

Method

The simplicity of the new method of treatment suggested its application in our series of 31 patients with secondary amenorrhea ranging in age from 15½ to 38 years with an average age of 23. As is seen in Table I, the duration of amenorrhea was from 2 months to 7 years. The disorder in all patients was due to pituitary or ovarian failure.

Treatment consisted of the administration of estradiol benzoate, 2.5 mg., and progesterone, 12.5 mg., which were drawn into one syringe and injected intragluteally; the same procedure was followed the ensuing day. In the chart application of this plan is shown in the columns "Therapy" and "Follow-up" respectively by merely indicating the days on which the injections were administered. Combined estrogenic-progestogenic therapy, differing in the plan of administration from the two-day treatment plan, is designated in the table as such. Estrogenic therapy alone, or progestogenic therapy alone, or stimulation therapy is similarly indicated in the table.

Results

Uterine bleeding resulted in 25 patients (80.6 per cent). In some instances (Cases 4, 5, 6, 10, 12) two courses of therapy were given and one patient (Case 8) received three series of two injections each. The total number of courses of treatment, 38, elicited 31 positive responses (81.5 per cent). In general, bleeding ensued 4 to 6 days following the second injection but there were also shorter as well as longer intervals. The amenorrhea in two of the 6 patients who failed to respond (Cases 1, 12, 18, 23, 27, 28) was of more than two years' duration. Four of these showed marked hypoplasia of the uterus. In four patients (Cases 17, 19, 20, 24), the first bleeding episode produced by the two-day treatment was followed by menstruation occurring spontaneously at four-

TABLE I. CLINICAL FEATURES OF 31 CASES OF SECONDARY AMENORRHEA AND RESULTS OF TREATMENT WITH THE TWO-DAY ZONDEK PLAN

NO.	PATIENT'S INITIALS	AGE	HT. IN.	WT. LB.	BODY BUILD	MENSTRUAL AND OBSTETRICAL HISTORY	DURATION OF AMENORRHEA	PELVIC (P.) OR RECTAL (R.) EXAMINATION	LABORATORY INVESTIGATIONS	THERAPY	BLEEDING EPISODE	FOLLOW-UP
1	Mrs. L. F.	38	61½	145	N. to S.	12x28x4	7 yr.	P.: Neg.	B.M.R. -10% End. biopsy: Resting phase	9 /2- 3/42	None	Did not report
2	Miss A. L.	27	62	130	N. to S.	15x28x7	4 yr.	R.: Neg.	B.M.R. +29%	9/22-23/42	10/ 2/42	Did not report
3	Miss M. G.	18	64¾	124	N. to S.	16x6 mo.-1 yr. x1	11 mo.	R.: Neg.	B.M.R. -8%	10/19-20/42	10/21/42	Did not report
4	Miss J. R.	16	63¾	130	N. to S.	13x6 mo. x5	10 mo.	P.: Neg.	B.M.R. -17%	11/18-19/42	11/26/42	12/22-23/42: bleeding 12/27/42
5	Miss A. K.	17	66¾	148	N. to S.	12x6 wk.-6 mo. x4	6 mo.	R.: Neg.	B.M.R. -5%	12/31/42-1/ 1/43	1/ 7/43	2/13-14/43: bleeding 2/21/43
6	Miss T. S.	18½	62	125	N. to S.	12x6 mo.-1 yr. x3	7 mo.	R.: Neg.		1/24-25/43	1/31/43	2/22-23/43: bleeding 2/28/43. Stimulation therapy: no response
7	Miss A. B.	16	60¼	90	N. to S.	12x28x7	3 mo.	P.: Neg.	B.M.R. -2%	2/ 2- 3/43	2/ 7/43	Did not report
8	Miss E. S.	17	60¼	107	N. to S.	12x4-6 wk x5-7	10 mo.	R.: Neg.	B.M.R. -2%	3/22-23/43	3/30/43	4/24-25/43: bleeding 4/29/43 9/21-22/43: bleeding 9/29/43
9	Mrs. B. W.	35	61	150	Obese	11x1-4 mo. x3 1 child, 8 yr. old	16 mo.	P.: Neg.		5/ 8- 9/43	5/15/43	Estrogenic therapy: bleeding 6/12/43. Spontaneous bleeding 8/6/43. 11/6-7/43: bleeding 11/15/43
10	Mrs. L. S.	30	60¼	150	Obese	18x1-4 mo. x3 2 children aged 8 yr. & 8 mo. respectively	9 mo.	P.: Parametritis	B.M.R. -10%	5/15-16/43	5/22/43	8/28-29/43: bleeding 9/4/43
11	Mrs. P. C.	24	67½	168	Obese, male escut.	11x28-5 mo. x3	6 mo.	Hypoplastic uterus; enlarged ovaries	B.M.R. -1% End. biopsy: Early proliferative phase	6/ 3- 4/43	6/ 9/43	Stimulation therapy: bleeding 8/18/43

12	Mrs. A. T.	24	62	128	N. to S.	14x28x31 Stillborn child 7 mo. previous	7 mo.	P.: Hypoplastic uterus	B.M.R. +4%	6/ 8- 9/43	None	Combined estrogenic progestogenic therapy: no response 7/10-11/43: no response
13	Mrs. M. M.	30	63½	170	Obese, male escut.	13x1 mo.-1 yr. x5	5 mo.	P.: Neg.	B.M.R. -15%	6/ 8- 9/43	6/15/43	Estrogenic therapy: bleeding 7/20/43 Spontaneous bleeding 9/27/43
14	Miss L. S.	16	63	126	N. to S	10x30x5	7 mo.	R.: Ovarian cyst?	B.M.R. -10%	6/ 9-10/43	6/16/43	Did not report
15	Miss G. B.	28	63½	123	N. to S.	16x3-6 mo. x3-4	5 mo.	R.: Neg.	B.M.R. +18%	6/10-11/43	6/18/43	Estrogenic therapy: bleeding 7/6/43 Stimulation therapy: bleeding 9/14/43
16	Miss H. G.	17	63	137	Male escut.	16x4 mo. x2 3 induced bleedings	2 mo.	R.: Neg.	B.M.R. +8%	6/13-14/43	6/22/43	Stimulation therapy: no response
17	Miss C. G.	18	60½	130	N. to S.	13x1-3 mo. x3	3 mo.	R.: Neg.	B.M.R. -9%	6/22-23/43	6/28/43	Spontaneous bleedings 7/26/43, 8/23/43, 9/20/43, 10/18/43, 11/16/43, and 12/30/43
18	Mrs. R. G.	25	61¼	199	Obese	11x28x3	5 yr.	P.: Hypoplastic uterus	B.M.R. +12%	6/25-26/43	None	Did not report
19	Miss H. K.	20	63¾	106	N. to S. hypomastia	15x6 wk.-6 mo. x7	2 mo.	P.: Enlarged right ovary	B.M.R. -9%	6/28-29/43	7/16/43	Spontaneous bleeding 8/28/43
20	Mrs. G. G.	23	61¾	123	N. to S.	11½x1-3 mo. x3-5	5 mo.	P.: Neg.	B.M.R. +3% End. biopsy: Proliferative phase	7/14-15/43	7/22/43	Spontaneous bleeding 9/7/43
21	Miss A. L.	25	64	142	N. to S.	12x1-6 mo. x4	4 mo.	P.: Parametritis		8/16-17/43	8/22/43	Stimulation therapy: bleeding 9/27/43
22	Miss M. G.	19	62	104	N. to S. Male escut.	17x2-8 mo. x2	7 mo.	P.: Neg.		8/17-18/43	8/23/43	Did not report
23	Mrs. L. P.	35	62	136	N. to S.	15x28-2 mo. x3	17 mo.	P.: Hypoplastic pelvic viscera		8/25-26/43	None	Stimulation therapy: no response

TABLE I—CONT'D

NO.	PATIENT'S INITIALS	AGE	HT. IN.	WT. LB.	BODY BUILD	MENSTRUAL AND OBSTETRICAL HISTORY	DURATION OF AMENORRHEA	PELVIC (P.) OR RECTAL (R.) EXAMINATION	LABORATORY INVESTIGATIONS	THERAPY	BLEEDING EPISODE	FOLLOW-UP
24	Miss B. O.	16	58	118	N. to S.	13x5-6 wk. x4	2½ mo.	P.: Neg.	B.M.R. -20%	9/ 7- 8/43	9/15/43	Spontaneous bleedings 10/12/43, 11/11/43, and 12/20/43
25	Miss D. S.	20	64½	110	N. to S. Male escut.	13x28x3 to age of 17; from there on irregular and longer intervals	8 mo.	R.: Neg.	B.M.R. +19%	9/15-16/43	9/21/43	Did not report
26	Mrs. H. B.	27	65	145	N. to S.	14x2-3 mo. x3 1 child aged 11 mo.	6 mo.	P.: Neg.	B.M.R. -10%	9/15-16/43	9/23/43	Did not report
27	Miss A. G.	29	65	120	N. to S.	16x6-8 mo. x2-3	17 mo.	P.: Hypoplastic uterus	B.M.R. -29%	9/22-23/43	None	Progestogenic therapy: no response
28	Miss J. S.	15½	66	142	Hypomastia	14x1-7 mo. x2	6 mo.	R.: Neg.	B.M.R. -18%	9/23-24/43	None	Did not report
29	Mrs. M. S.	24	63¼	123	N. to S.	16x28x2-3 1 miscarriage 3 yr. ago	3 mo.	P.: Oophoritis and parametritis	B.M.R. -10%	10/ 3- 4/43	10/10/43	Did not report
30	Mrs. C. D.	23	68	183	Obese	16x3-8 mo. x8-14	4 mo.	P.: Small uterus; right ovarian tenderness	B.M.R. -13%	10/16-17/43	10/20/43	Did not report
31	Miss G. S.	20	63¾	132½	Normal	13x6 wk.-5 mo. x3	3 mo.	R.: Neg.	B.M.R. +13%	10/25-26/43	11/ 2/43	

week intervals. Two of these patients (Cases 19, 20) reported one such bleeding; one girl (Case 24) menstruated three times and one (Case 17) had six spontaneous consecutive periods. There were spontaneous bleeding episodes also in other patients of the series but these had received other therapeutic measures intermittently and therefore their spontaneous responses are not detailed here. While it is not to be expected that hormonal therapy of but two-days' duration—regardless of its efficacy in producing bleeding—would alter the pattern of the endometrial mucosa, it was desirable to study pre- and postmedication endometrial biopsy specimens in some patients.

The following history of a patient exemplifies both procedure and observations in this series.

Case Report

Mrs. P. C., white, aged 23, married 2½ years, was first seen on April 27, 1942. Her chief complaints were sterility and protracted periods of amenorrhea for the past eight years.

Past History: Menarche was at the age of 11. Periods were regular for 4 years, occurring every 28 days and lasting from 4 to 5 days. Since the age of 15, however, menstruation occurred only every 4 to 6 months. Coincidental with this oligomenorrhea she noticed a gradually increasing hypertrichosis of the face, chest and abdomen, decreased vitality and frequent attacks of abdominal pain. The patient had had mastoiditis and pyelitis at the age of 10; no other serious illness or operation was reported. A congenital defect of both eyes (conical cornea) had been noted by an ophthalmologist several years previously and this was confirmed by Dr. Andrew Rados on May 8, 1942. During the past 4 years, the patient had medical attention for amenorrhea and sterility and received intensive hormonal therapy to which she responded occasionally by staining. The last episode of staining in November, 1941, was brought on by intensive estrogenic therapy.

Physical Examination: Height 67½ inches, weight 168 pounds; patient exhibited some traits of masculinity such as hirsuties of the face, chest and extremities. The blood pressure was 130/70 mg. Hg and the pulse rate 56. The urinalysis was negative for albumin and sugar. A study of the blood chemistry revealed the following findings: sugar, 113 mg. per cent; cholesterol, 180 mg. per cent; and uric acid, 1.5 mg. per cent. The basal metabolic rate was normal (minus 1 per cent). Pelvic examination revealed an enlarged clitoris (2½ cm.), a narrow vaginal orifice and a hypoplastic uterus. The cervix was elongated so that the cervix-body ratio was 2:1. Both ovaries were enlarged and apparently cystic.

The patient was subjected to estrogenic therapy which elicited bleeding in June, 1942. In view of the presence of signs of masculinization (hypertrophy of the clitoris, hirsutism), it was decided to perform an exploratory laparotomy with the object of determining the presence or absence of testicular tissue or any masculinizing tumor. The operation performed on July 15, 1942, by Dr. Charles Robbins, disclosed enlarged sclerotic ovaries and a chronically inflamed appendix. The adrenal glands were palpated but no enlargement could be detected. A wedge-shaped excision of the midportion of both ovaries and an appendectomy were carried out. The patient's recovery was uneventful. Histologic examination of the resected ovarian tissue revealed several

Fig. 1.—Case 11, premedication endometrial biopsy showing proliferative phase.

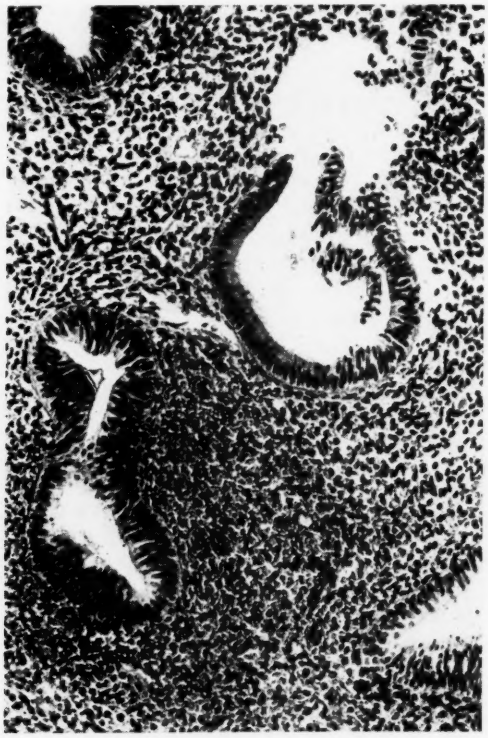

Fig. 2.—Case 11, postmedication endometrial biopsy showing proliferative phase.

immature follicular cysts and corpora albicantia; there was also evidence of increased fibrosis.

Since resumption of menstruation did not occur following the operation, the patient received both stimulative and substitutive hormonal therapy for a period of 6 months. Bleeding episodes resulted, however, from substitution therapy only. The last period elicited by estrogen-progestogen therapy having occurred on March 31, 1943, it was decided to subject the patient to the simplified two-day treatment. This was also advisable since she moved out of town and was unable to make frequent visits to the office. On June 3, more than 2 months after the last injection of any hormonal preparation, a premedication endometrial biopsy was taken. The histologic picture of the specimen was typical of an early proliferative phase (Fig. 1). Immediately after obtaining the biopsy specimen, estradiol benzoate, 2.5 mg., and progesterone, 12.5 mg., were administered, and the same dose was repeated the following day. The postmedication biopsy specimen taken on June 5, revealed no change as compared with the biopsy specimen of two days previously—the pattern was again that characteristic of the proliferative phase (Fig. 2). Therapy resulted in uterine bleeding on June 9. No further spontaneous periods occurred.

Discussion

When Zondek, Rozin and Vesell[3] demonstrated that there was no need for inducing complete proliferation of the endometrium with estrogens in order to elicit uterine bleeding with progesterone, the groundwork was laid for further simplification of effective treatment of secondary amenorrhea. The obvious advantage of the 2-day treatment plan subsequently devised by Zondek as compared with the heretofore commonly employed method of treatment devised by Kaufmann[4] can be clearly demonstrated by comparing a table, as given by Kaufmann (Table II), portraying a general outline for a treatment plan of amenorrhea and a table (Table III) depicting similarly the two-day Zondek technique. As can be easily seen, Kaufmann advocates no less than 10 injections, 5 consisting of estradiol benzoate, 5 mg. each, and an equal number of progesterone, 5 mg. each, spaced over a period of more than 3 weeks, with the expectation that menstruation will be produced on the twenty-fifth day after initiation of treatment. The Zondek plan, on the other hand, calls for 2 injections only to be given on consecutive days with a total requirement of 5 mg. estradiol benzoate and 25 mg. progesterone. While the amounts of progesterone needed are identical for both techniques, the Zondek plan obviates the use of large doses of estrogen, i.e., only 5 mg. of estradiol benzoate as contrasted with 25 mg. administered according to Kaufmann's recommendations. Moreover, the fact that large doses of estrogen may have an inhibitory effect on the anterior pituitary must be considered. Finally, shortening of the duration of therapy from 25 days to 6 days (2 days for actual treatment and averagely 4 days before onset of bleeding) is of great value in many instances.

TABLE II

SUNDAY	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY	SATURDAY
	1	2	3	4	5	6
7	8	9	10	11	12	13
14	15	16	17	18	19	20
21	22	23	24	25	26	27

Estradiol benzoate, 5 mg. Progesterone, 5 mg. Menstruation

Kaufmann's table (loc. cit.) portraying his treatment plan of amenorrhea.

TABLE III

SUNDAY	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY	SATURDAY
	1	2	3	4	5	6
7	8	9	10	11	12	13
14	15	16	17	18	19	20
21	22	23	24	25	26	27

Estradiol benzoate, 2.5 mg. + progesterone, 12.5 mg.

Uterine bleeding

Table portraying Zondek's two-day treatment plan of amenorrhea.

Zondek suggested that the 2-day treatment plan be restricted to cases of less than 2 years' duration. That such limitations should be considered is borne out by the fact that in two of our nonreactors, the amenorrhea was of more than 2 years' duration. On the other hand, in Case 2 of the series presented the amenorrhea was of 4 years' standing—nevertheless, the patient responded promptly to the two-day treatment plan. The comparative results recorded by Zondek, by Berlind, and by us are shown in Table IV.

TABLE IV. COMPARATIVE RESULTS WITH ZONDEK'S TWO-DAY TREATMENT PLAN

	NO. OF CASES	NO. OF POSITIVE RESULTS	PER CENT
Zondek	17	11	64.7
Berlind	7	7	100.0
Present series	31	25	80.6

Summary and Conclusions

A series of 31 patients with secondary amenorrhea due to pituitary or ovarian deficiency is presented and the results with the simplified two-day treatment plan described. This method devised by Zondek consists of the injection of a combination of estradiol benzoate, 2.5 mg., and progesterone, 12.5 mg., on two consecutive days. Uterine bleeding was produced in 25 patients (80.6 per cent). Among the 6 nonreactors were 4 patients with marked uterine hypoplasia. In two of the unresponsive patients, the amenorrhea had persisted for more than 2 years. By restricting the simplified treatment plan to patients with an amenorrhea of less than 2 years' duration, the percentage of favorable responses (80.6 per cent in our series) can probably be further increased. No marked changes were produced in the endometrial pattern with the 2-day treatment as evidenced by the pre- and postmedication biopsy specimens which are presented.

The advantages of the simplified method are discussed. The 2-day treatment plan should be employed in all those instances of functional amenorrhea of less than 2 years' duration where thyroid medication has failed to yield results and where for some reason or another, it is desirable or imperative to obtain uterine bleeding in as short a period of time as possible.

Acknowledgment: The special combination packages for the simplified two-day treatment of amenorrhea consisting of 2 ampoules of Dimenformon Benzoate (each representing 2.5 mg. of estradiol benzoate) and 2 ampoules of Progestin (each representing 12.5 mg. of progesterone), employed in this study, were liberally supplied by Roche-Organon, Inc., Nutley, New Jersey, through the courtesy of Dr. Leo Pirk.

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CORD TRANSFUSIONS IN NEWBORN INFANTS*

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GREAT emphasis has been placed on the prevention of maternal mortality, with considerable success. Today it seems fitting to turn our attention to the mortality among infants, where a proportionate success is still to be achieved.

The greatest loss of life among infants is during the first twenty-four hours, and Holt and McIntosh[1] state that "if the infant survives for the first forty-eight hours after birth its chances are immeasureably improved; various clinics have reported [mortality] rates of 3 to 9 per cent if these early deaths are excluded."

The responsibility for the first twenty-four hours is the obstetrician's; deaths in that period come under the obstetric, not the pediatric, service. Thus the question arises, what can be done by the obstetrician to increase the chances of newborn infants to survive the first forty-eight hours? The usual treatment suffices if the babies are full term and if they are not suffering from the effects of a long labor or some blood dyscrasia. But for prematures, infants affected by difficult labor and those with hemorrhagic disease or erythroblastosis, special treatment must be instituted, and the sooner the better.

This paper presents a method of transfusion with citrated adult blood given immediately after birth through the umbilical vein. The procedure is prophylactic in cases of prematurity, difficult labor and a history in the mother of previous stillbirths, prematures and early deaths.

In 1937, Wilson[2] reported the use of lobelin by way of the umbilical vein in cases of difficulty in spontaneous respiration and described in detail the method of administration. After using lobelin in this way in several cases, it occurred to the writer that adult blood might be given by the same route, particularly for prematurity. Such a transfusion was first given at the Methodist Hospital in Brooklyn in 1940, and the case was reported before the New York Obstetrical Society the same year. The infant, which survived, weighed 4 pounds, 4 ounces and was of 28 weeks' gestation; the mother had lost two previous premature infants (see Case Report 1, Mrs. D. A.). In the next two years 5 more cord transfusions were done in prematures, and in 1943, 12, a total of 18 cord transfusions in prematures in a four-year period. In addition

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in 1943, the method was used in 16 full-term infants, making a total of 34 cord transfusions in newborn infants from 1940 through 1943.

Three tables follow. Table I gives maternal and fetal mortality statistics at the Methodist Hospital in Brooklyn for the four years, 1940 through 1943. Table II is a summary of the 18 transfusions in prematures, and Table III of the total 34 transfusions.

TABLE I. MATERNAL AND INFANT MORTALITY STATISTICS
METHODIST HOSPITAL 1940-1943

				LIVING INFANTS*			INFANT DEATHS		
YEAR	TOTAL DELIVERIES	MATERNAL DEATHS	STILLBIRTHS	FULL TERM	PREMATURE	TOTAL	FULL TERM	PREMATURE	TOTAL
1940	1,726	2	68	1,601	72 (1)	1,673 (1)	9	23	32
1941	1,865	2	77	1,722	88 (3)	1,810 (3)	13	18 (1)	31 (1)
1942	2,086	3	84	1,922	100 (2)	2,022 (2)	16	20	36
1943	2,167	2	94	1,999 (16)	94 (12)	2,093 (28)	7 (1)	20 (2)	27 (3)
Total	7,844	9	323	7,244 (16)	354 (18)	7,598 (34)	45 (1)	81 (3)	126 (4)

*Many of the premature infants were nonviable, but if they breathed following delivery they were included in this table.

( ) Numbers in parentheses indicate infants given cord transfusions.

Results

The 18 infants classified as prematures weighed under 5½ pounds, and gestation with one exception was from 23 to 36 weeks. The exception was a twin weighing 4 pounds, 14 ounces, gestation 39 weeks. There were 3 deaths among the prematures, a mortality of 16.6 per cent. Mother's blood was used in 16 with 2 deaths, one in a nonviable infant; father's blood was used in 1; professional donor's blood was used in 1, with death of the infant.

Four of the prematures weighed less than three pounds and the only one to die weighed 1 pound, 6 ounces. Five weighed from three to four pounds, and the only one lost followed a breech delivery. Weight of the infant was 3 pounds, 11 ounces; 30 c.c. of mother's blood were given. The infant lived 15 hours; blood was aspirated from the throat. Nine weighed from four to five and a half pounds, and the one death in this group was an infant whose mother was Rh–, father Rh+. Weight was 4 pounds, 1 ounce. The infant was transfused with 20 c.c. of Rh– blood from a professional donor. The baby did well until the second day, when it began to show signs of cerebral hemorrhage and died the following day; autopsy revealed a massive cerebral hemorrhage.

The results in these cases may be compared with Stander's mortality figures for premature infants: 100 per cent for weight less than 1,000 grams, 65.6 per cent from 1,000 to 1,500 grams, and 25 per cent from 1,500 to 2,000 grams.[3] They may also be compared with Holt and McIntosh's figures for prematures under ideal hospital conditions: 95 per cent for weight less than 1,000 grams, 67 per cent from 1,000 to 1,500 grams, and 25 per cent from 1,500 to 2,000 grams. The mortality rate for prematures at the Methodist Hospital, 1940 through 1943, all weights under 5½ pounds, including these 18 cases, was 22.8 per cent (81 deaths among 354 living prematures).

TABLE II. CORD TRANSFUSIONS IN 18 INFANTS WEIGHING LESS THAN 5½ POUNDS

WEIGHT POUNDS	WEIGHT OUNCES	GESTATION	AMOUNT OF BLOOD	REMARKS
1	6	23 weeks	20 c.c.	Died in 35 minutes. Nonviable.
2	7	26 weeks	30 c.c.	Hb. 21.7 Gm., reds 6,280,000 at birth. At 6 months weighed 11 pounds.
2	14	28 weeks	15 c.c.	Critical at birth, respirations intermittent, periods of apnea.
2	15	32 weeks	30 c.c.	Died at 3 months of strangulated hernia. Not a neonatal death.
3	2	28 weeks	30 c.c.	Color poor, prognosis guarded. Hb. 22.4, reds 6,000,000.
3	9	34 weeks	20 c.c.	Critical. Hb. 150%, reds 6,200,000. At one month weighed 5 pounds 5 ounces.
3	11	32 weeks	30 c.c.	Died within 15 hours. Critical, breech. Blood aspirated from throat.
3	12	33 weeks	35 c.c.	One of twins. Red cells 7,500,000. Other twin, 5,500,000.
3	13	33 weeks	20 c.c.	Mother Rh+, father Rh–.
4	1	32 weeks	20 c.c.	Critical at birth. Discharged in 25 days weighing 5 pounds 4 ounces.
4	1	36 weeks	20 c.c.	Died on the third day. Mother Rh–, father Rh+. Blood from professional donor used. Autopsy showed massive cerebral hemorrhage.
4	3	32 weeks	35 c.c.	Apparently about 6 months' gestation. Critical at birth.
4	4	28 weeks	40 c.c.	Mother had lost two premature infants. Father's blood used.
4	6	33 weeks	20 c.c.	Critical for several days. Hb. 19 Gm., reds 8,000,000.
4	13	32 weeks	30 c.c.	Previous delivery by cesarean. Spontaneous delivery. Fair at birth.
4	14	36 weeks	20 c.c.	Mother toxic. Red cells 7,500.000
4	14	39 weeks	20 c.c.	Twin. Hb. 16 Gm., reds 7,050,000, 35% nucleated red cells. In 6 days Hb. 16.5 Gm., reds 5,000,000, occasional nucleated red cell.
5	5	36 weeks	18 c.c.	Hb. 24 Gm., reds 6,550,000.

NOTE: In several of the above cases the transfusion should have been larger. This is especially evident in the case of the 4-pound, 1-ounce infant, mother's blood Rh–. A transfusion of 40 or 45 c.c. might have saved this baby.

TABLE III. TOTAL CORD TRANSFUSIONS

	TOTAL	LIVED	DIED	REMARKS ON DEATHS
Under 2 pounds	1		1	Lived 35 minutes. Nonviable. Weight 1 pound 6 ounces. Given 20 c.c. mother's blood.
2 to 3 pounds	3	3		
3 to 4 pounds	5	4	1	Lived 15 hours. 32 weeks. Breech. Critical at birth. Given 30 c.c. mother's blood. Blood aspirated from throat.
4 to 5½ pounds	9	8	1	Lived 3 days. Mother Rh–, father Rh+. 20 c.c. blood from Rh– professional donor used. Autopsy showed massive cerebral hemorrhage.
5½ pounds and over	16	15	1	Lived 25 minutes. Weight 6 pounds, 4 ounces. 36 weeks. Both parents Rh+. Autopsy showed hemorrhagic disease of the newborn.
Total	34	30	4	

NOTE: There were 31 viable babies transfused with mother's blood with only one death.

Case Reports

CASE 1.—Mrs. D. A. had lost two babies, one at 8 months' gestation which lived for 12 hours, another at 7 months which lived for 5 hours. There was no autopsy in either case; cause of death was given as prematurity and atelectasis.

Mrs. D. A. was admitted to the Methodist Hospital on September 1, 1940, in active labor. Gestation was 7 months. No sedatives were given and only a small amount of nitrous oxide for the delivery. The baby weighed 4 pounds, 4 ounces at birth, and 40 c.c. of the father's blood were given by cord transfusion. The infant lived, and now at the age of 3 is a normal child.

(For fourth child, see Case Report 3.)

CASE 2.—Mrs. A. W. was admitted to the hospital October 16, 1941. She was a para i, aged 37. Gestation was only 26 weeks. Delivery was breech, birth weight 2 pounds, 7 ounces, red cells 6,280,000, Hb. 128 per cent, baby's condition at birth critical. Thirty cubic centimeters of mother's blood were given by cord transfusion. The infant was discharged from the hospital January 2, 1942, weighing 5 pounds, 2 ounces. At the age of 6 months weight was 11 pounds. This is the smallest baby in the series of prematures to survive.

In 1943, cord transfusions were given to full-term infants as well as to prematures. In the 16 infants weighing 5½ pounds and over and classed as full terms, the indications for cord transfusion were: difficult forceps deliveries, 10; difficult breech extractions, 3; previous loss of infant, 2; twin, 1. There was one death in this group. A previous premature had survived, the first in the series of 18 prematures given cord transfusions; two prematures before that had died. This infant weighed 6 pounds, 4 ounces, gestation 36 weeks, thus a premature in spite of size. Twenty cubic centimeters of father's blood were given, but the infant lived only 25 minutes; autopsy revealed death from hemorrhagic disease (Case Report 3, Mrs. D. A.).

Mother's blood was given in 15 cases, father's blood, in which the death occurred, in 1.

CASE 3.—Mrs. D. A. For previous history see Case Report 1.

This mother had her fourth child in June, 1943. Gestation was 36 weeks, weight 6 pounds, 4 ounces. The infant was transfused with 20 c.c. of its father's blood, but lived only 25 minutes. Autopsy showed it died from hemorrhagic disease. Both parents were Rh+.

CASE 4.—Mrs. M. D. had lost two babies, both full term. The first died during delivery; the cord smear showed 30 per cent normoblasts. The second had been transfused (not a cord transfusion) with 50 c.c. of its father's blood but lived for only 36 hours. This infant also had 30 per cent normoblasts in the cord blood.

On August 18, 1943, this patient was delivered of a baby weighing 6 pounds, 14 ounces. There were 73 per cent normoblasts in the cord blood. It was given 40 c.c. of mother's blood by cord transfusion. On the fifth day the normoblasts were only 5 per cent. The infant made an uneventful recovery. Both parents were Rh+.

Technique

The administration of blood by way of the umbilical vein is a very simple procedure. The citrated blood to be given should be in readi-

ness before the baby is delivered. A 50 c.c. syringe is used in which are 5 c.c. of a 2 per cent solution of sodium citrate. The blood is withdrawn and the syringe tilted several times to mix the citrate solution with it. If the mother is toxic, or if for any other reason her blood is not desirable, blood from the father, some other donor or from the bank if it is available may be used. Preserved blood should be filtered through several layers of gauze before being administered.

As soon as the baby is born and before cutting the cord, the umbilical vein is easily identified and may be entered with the same needle used to withdraw the blood. If preferred a cannula may be placed in the vein. The transfusion should be started as far from the baby as possible. This serves two purposes: if the vein is not easily entered another attempt can be made nearer the baby; if the baby should move the needle will not be disturbed. As soon as the transfusion is started the cord should be clamped between the needle and the placenta. If it is decided to cut the cord before giving the transfusion, the cord may be gently compressed with the fingers near the umbilicus so that the veins remain distended until the transfusion is started.

The transfusion should be given slowly, 30 or 40 c.c. in about five minutes. If the operator is dubious about embarrassing the child's circulation with too many erythrocytes, as soon as the baby is delivered the cord is clamped so as not to allow the placental blood to enter the baby, since the amount of placental blood that could be milked into the baby from the cord would amount to as much as or more than that given by the transfusion, and the transfusion is then started.

If there is any delay, as in drawing the blood from the donor or in starting the transfusion, it may be impossible to get the blood to flow through the cord. If there has been considerable trauma to the cord during delivery, transfusion via the cord may be impossible.

There has been some discussion as to the amount of blood that should be given. For premature infants, in whom the purpose of the transfusion is to provide a medium for the carrying on of the circulation, a considerable amount would seem to be indicated, and pediatricians recommend 15 to 20 c.c. per kilogram of baby weight. As much as 150 c.c. may be given a full-term baby if it has had a hemorrhage or if it is suffering from hemorrhagic disease of the newborn. Such large transfusions may cause some cyanosis, but otherwise do not seem to affect the infant. In our series of prematures in a number of cases we felt that more blood might have been given, and in one case at least might have saved the life of the child.

A striking phenomenon occurring during cord transfusions, the cause of which is still to be investigated, is the blanching of the cord during the transfusion, the veins apparently collapsing.

Rationale of the Method

When a baby is premature, it often seems, at first, like a normal but small infant. The color is good; the cry and the respirations are usually spontaneous. The obstetrician, thinking the infant will survive, orders premature care, shifting responsibility to the pediatrician, who may not see the child for twelve or even twenty-four hours after delivery. A few hours after delivery the baby becomes cyanotic, its condition critical, and death ensues.

In prematurity, nature has not had sufficient time to complete preparations for extrauterine life. It may be assumed that the immature red corpuscles are not accustomed or able to gather the oxygen from the lungs, carry it to the body tissues and bring back the carbon dioxide and release it in the lungs. This fact may very well account for the early cyanosis. The use of any stimulation, clyses or the administration of oxygen has little effect in the premature infant. But the administration of adult blood immediately following delivery, by way of the umbilical vein, gives the infant an adult tissue that enhances the baby's chances for survival because the blood not only acts as nourishment, but also stimulates respiration and helps to overcome cyanosis. In the premature, the need for nourishment and stimulation in the first few hours after birth is urgent.

One of the most serious difficulties for premature infants is hemorrhage. Porter and Carter,[4] and Holt and McIntosh claim that many premature infants and almost all of those weighing under 1,000 grams suffer from intracranial bleeding. According to Holt and McIntosh, the fragility of the blood vessels is greater than in the full-term infant, and the concentration of prothrombin less. Porter and Carter believe that a deficiency of vitamin K and of prothrombin storage during fetal life is closely associated with hemorrhagic disease in the newborn infant. Before the administration of vitamin K to all patients in labor was adopted at the Methodist Hospital, it had been our routine practice when a delivery was extremely difficult to give the infant blood subcutaneously to forestall any tendency to hemorrhage. It would seem that in hemorrhage or tendency to hemorrhage occurring in spite of the vitamin K administration, if subcutaneous injection of blood would be of assistance, intravenous transfusion of blood would have even more benefit.

When blood is given to the newborn infant which shows some evidence of shock with poor respirations, it is surprising how often the respirations are stimulated after the cord transfusion. The time at which change in respiratory rate takes place seems to correspond to the time it would take the blood to reach the respiratory center. In adults, the effect of transfusions of blood or plasma in shock with or without hemorrhage is well recognized.

Prompt transfusion is most important in infants suffering from erythroblastosis. The number of normoblasts may be only slightly increased at birth, but unless transfusion is done at once, they multiply very rapidly and repeated transfusions may be needed to save the life of the child.

According to Levine et al.,[5] if the mother gives a history of stillbirths, miscarriages or of infants dying soon after delivery, tests for the Rh factor should be carried out early in pregnancy so that at the time of delivery if the mother is Rh negative, the infant may be transfused with blood from an Rh– compatible donor.

So far as the question of compatibility is concerned, Levine, in a personal communication,[6] states as follows:

"With regard to compatibility tests it is significant that the newborn infant's blood contains no isoagglutinins characteristic of its blood group. Any agglutinins which are demonstrable are derived from the mother. Accordingly, one transfusion may be given without resorting either to blood grouping or to compatibility tests. Should the mother's blood be incompatible, it is certain that the blood will survive long enough to exert its beneficial effect on the newborn infant. However, this transfusion serves to immunize the infant so that the following transfusions, if required, must be carried out with compatible blood of the same blood group as the infant's. Although the mother's blood may be given indiscriminately for one transfusion, it seems preferable to use any blood of group O.

"As already indicated [reference to Levine et al.] the erythroblastotic infant of an Rh negative mother should be transfused with random Rh negative blood which is otherwise compatible."

Comparison may be made among the infants in three sets of twins, two in the premature series, one in the full term. In each set the second twin was transfused. In the two transfused infants from the premature series the red cells were about 2,000,000 higher than in the untreated mate and the hemoglobin correspondingly higher. In addition one of these transfused twins (weight 4 pounds, 14 ounces, 39 weeks' gestation) had 35 per cent normoblasts in its blood, while its mate had only an occasional nucleated red cell. In six days in this infant the count was normal, and the red cells dropped from 7,050,000 to 5,000,000. In the other treated twin, however (weight 3 pounds, 12 ounces, gestation 33 weeks, red cells at birth 7,000,000), the red cells six days later were still 7,000,000.

All of the babies lived, but in each case the transfused infants were much more active. There was little difference in their gain in weight.

Discussion

I have been unable to find any mention in the literature of the umbilical cord as an avenue for the routine transfusion of the baby in the delivery room. Sidbury[7] in 1923 reported a case in which the attending physician had done a dorsal slit on an infant, and it had bled for four days. A wet dressing of boric acid was applied to the cord, and eight hours later the cord was cut proximal to the ligature, a regular transfusion needle was inserted into the umbilical vein and when no resistance was felt on the injection of saline, 100 c.c. of mother's blood were transfused. As far as Sidbury knew this method had never been used before. Marriott,[8] 1936, states: "In infants of two days old, particularly when suffering from hemorrhagic disease, the umbilical vein may be entered quite readily after removing the ligature around the cord."

For simplicity the method has no comparison with any other method of giving transfusions to newborn infants. It is possible for one skilled in using the scalp veins to do such transfusions in some infants, but in many the veins are small and difficult to enter, and it is even more difficult to keep the needle in the vein long enough to give the required amount of blood. In desperation the physician will endeavor to give the blood by way of the longitudinal sinus. The location of the sinus is not constant, and not infrequently the blood is given subdurally and death of the infant results.

In a paper published in 1924, I[9] described a method of transfusing newborn infants by way of the median basilic vein, and during the next twelve years more than 100 such transfusions were given. It was found that when the transfusions were given early, the infant usually lived, mortality increasing with the number of days of delay. Transfusions given the day following delivery may be too late to save the baby, and they may be even further delayed by search for a compatible donor and waiting for a convenient time when a physician experienced in transfusing infants may give the transfusion.

In defining prematurity, we are confronted with many borderline cases. On the basis of weight alone some infants are classified as prematures when actually they are full term or nearly so. An example is the twin in the series of 18 prematures, weight 4 pounds, 14 ounces, gestation 39 weeks. Such babies usually survive. On the other hand, there are the infants that, judged by weight, are classified as full term whereas on the basis of gestation they are really premature. Among the 16 "full-term" infants given cord transfusions, 3 had a gestation of 36 weeks or less, and the only one in the series to die was of this type. Weights at full term in such infants might have been eight, nine, even eleven pounds, and the question arises as to the probable weight at seven months' gestation of an infant weighing eleven pounds at term. In the case of these infants we are likely to ignore the possibility of prematurity, fail to order premature care, and the infants die. Such infants should always be treated as prematures, and cord transfusion as a prophylactic procedure should apply equally to large and small prematures.

The method suggests usefulness in salvaging prematures delivered by cesarean section. In 1943 at the Methodist Hospital 9 cesarean sections were done while the infant was premature. The smallest weighed 3 pounds, 2 ounces, the largest 5 pounds, 7 ounces. Five of these babies died, a mortality of 55 per cent. None was transfused. Although cesarean sections are frequently done solely in the interest of the premature infant, such infants are often lost.

Summary

The umbilical vein offers a convenient avenue by which newborn infants may be transfused with adult blood in the delivery room im-

mediately after birth. Citrated mother's blood has been used in most cases to date; father's or donor's blood or blood from the bank may serve as a substitute. A little less than 10 c.c. per pound of baby weight is sufficient. The technique is simple.

Premature infants and particularly those usually considered nonviable are definitely benefited.

In infants suffering from difficult delivery and those in doubtful condition, a small transfusion of 20 c.c. of mother's blood acts as a direct stimulation to the respiratory center and tends to overcome any tendency toward hemorrhage.

If the mother gives a history of previous stillbirths or if hemorrhagic disease or erythroblastosis is suspected, cord transfusions may be of benefit.

Thirty-four cases of cord transfusion are reported, 18 in infants weighing less than 5½ pounds, gestation from 23 to 39 weeks, 16 in infants weighing 5½ pounds and over, 13 full term, 3 with gestation of 36 weeks or under. There were 4 deaths, 3 in the smaller weight group, 1 in the larger.

This is a preliminary report of a simple, apparently harmless procedure which may be the means of saving more premature babies, of benefiting full-term infants when the delivery has endangered life, and of treating the blood dyscrasias.

The writer wishes to express his gratitude to Dr. Philip Levine for his personal note and for his helpful suggestions in the editing of this paper. The majority of the cord transfusions were done by Dr. Everado Goyanes and Dr. Isabel Seissman, our residents in obstetrics.

Note.—There were 24 additional cord transfusions during the first 2½ months of 1944. Nine of the babies were premature, with two deaths. The mother of one had a premature separation of the placenta and the baby lived for 5 hours. The other lived for 4 days following a breech delivery, accidental hemorrhage was from a low implantation of the placenta; the cause of death was intracranial hemorrhage. There were 15 babies weighing more than 5 pounds, 8 ounces. To date, the total number of cord transfusions is 58, with six deaths.

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THE PROGNOSIS AND MANAGEMENT OF PREMATURE RUPTURE OF THE MEMBRANES*

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THERE have been several papers written in the past decade which emphasized the fact that premature rupture of the membranes is not a complication of obstetrics and therefore, the so-called "dry labor" is not a condition to be feared. However, because dry labor was so emphasized in the past and because many of the textbooks are slow in adapting the newer concept, it may be well to review again a series of cases showing the results which have occurred following premature rupture and thereby draw some conclusions as to the proper management of this condition.

Material

In order to secure a representative group of patients the cases used in this series were taken from two hospitals: First, a large maternity hospital, the staff of which consists of men trained and specializing in obstetrics and gynecology; and second, a smaller general hospital with an obstetrical staff but with many general practitioners doing "occasional obstetrics." Both ward and private patients were used to eliminate variation in economic, physical and nutritional factors. The cases used were all women delivered in these two hospitals from Jan. 1, 1942, to July 1, 1943.

TABLE I

Total number of patients delivered	4,806
Total number of infants	4,859
Total number of patients with premature rupture of the membranes	636
Total number of infants	645

The total number of patients delivered in these two institutions during this period was 4,806. There were 53 sets of twins resulting in a total of 4,859 infants. Of these patients, 636 or 13.2 per cent had definite rupture of the membranes before the onset of labor pains. It is unreliable to use this as an absolute incidence because the diagnosis of rupture of the membranes was based on clinical evidence alone. Other cases probably had ruptured membranes but were discarded because their histories were not definite. This series also includes 12 cases of artificial rupture performed for induction of labor.

Of these 636 patients, 117 or 18.4 per cent began to have labor pains within an hour of the time of the rupture of the membranes. In these cases rupture of the membranes was probably the initial sign of the onset of labor. The majority of patients began to have labor pains within

*Read at a meeting of the Philadelphia Obstetrical Society, March 2, 1944.

1 to 6 hours of the time of rupture of the membranes. Twenty patients had a latent period of more than 72 hours before the onset of labor, the longest latent period being 63 days.

TABLE II. PERIOD OF TIME BETWEEN RUPTURE OF THE MEMBRANES AND THE ONSET OF LABOR

LATENT PERIOD	NO. OF PATIENTS	%	NO. OF INFANTS
0 to 1 hour	117	18.4	119
1 to 6 hours	262	41.2	267
6 to 12 hours	112	17.6	113
12 to 24 hours	77	12.1	78
24 to 48 hours	34	5.3	34
48 to 72 hours	14	2.2	14
Over 72 hours	20	3.1	20
Total	636		645

The factors most feared in the management of patients with premature rupture of the membranes have been (1) prolongation of the first and second stages of labor, (2) increased incidence of operative deliveries, (3) sepsis and (4) injury to the fetus.

Length of Labor

TABLE III

	NORMAL	MEMBRANES RUPTURED	MEMB. RUPT. OVER 24 HR.	OCCIPUT POST.	BREECH
Primiparas	18.0 hr.	11.6 hr.	11.4 hr.	16.2 hr.	12.0 hr.
Multiparas	12.5 hr.	7.9 hr.	9.6 hr.	12.3 hr.	7.0 hr.

Textbooks quote the average length of labor as eighteen hours for primiparas and twelve and a half hours for multiparas. In this series the patients with ruptured membranes averaged 10.2 hours for the first and second stages of labor, 11.6 hours for primiparas and 7.9 hours for multiparas. It might be expected that labor would be lengthened to a greater degree in patients with occiput-posterior positions and breech presentations but even these patients had a shorter labor than the normal usually quoted. It is difficult to compare these findings with the stated normal length of labor because in both institutions the use of prophylactic forceps is routine, thereby shortening the second stage of labor, but it is safe to conclude that labor is not lengthened by premature rupture of the membranes.

In the 68 cases with membranes ruptured over 24 hours before the onset of labor, the average length of the first and second stages of labor was 11.4 hours for primiparas and 9.6 hours for multiparas. Therefore, there does not seem to be any relationship between the length of the latent period before the onset of labor and the length of labor.

These observations serve to invalidate the theory that the bag of waters is necessary for efficient dilatation of the cervix. If this concept was true, then premature rupture of the membranes would certainly result in a lengthening of the first stage of labor. DeLee and Greenhill

state in their textbook that the best time for the membranes to rupture is when the cervix is completely dilated and effaced, but this does not seem to be justified. The unruptured membranes probably bulge into and through the dilating cervix because this is the point of least resistance rather than having any hydrostatic action.

Incidence of Operative Deliveries

TABLE IV

OPERATIONS	TOTAL SERIES	%	RUPTURED MEMBRANE	%
Forceps	2,794	57.5	401	62.1
Low	2,601	53.5	383	59.2
Mid	188	3.8	18	2.8
High	5	0.1	1	0.1
Breech extraction	123	2.5	16	2.4
Version and extraction	31	0.6	5	0.7
Cesarean section	268	5.5	7	1.0
Total operations	3,216	66.1	429	66.4

The incidence of operations in the total series and in the group with premature rupture of the membranes was almost identical. There was a slight increase in the incidence of low forceps operations in the group with ruptured membranes. The incidence of cesarean section was greater in the total group, as might be expected since many of these cases in this group were elected at some time before the expected date of delivery allowing less opportunity for rupture of the membranes. The indications for the seven cesarean sections performed on the patients with premature rupture of the membranes were as follows:

1. Large breech. Membranes ruptured before elective section. No labor.
2. Disproportion. Membranes ruptured before elective section. No labor.
3. Previous cesarean section.
4. Cervical dystocia.
5. Premature rupture of the membranes given as the indication. Failure of several attempts at medical induction and surgical induction with bag. Porro section.
6. Fibroid obstructing delivery.
7. Disproportion. Eight-hour test of labor.

In only one of these cases was premature rupture of the membranes thought to be a factor inhibiting normal progress.

An analysis of the patients with premature rupture of the membranes reveals that there were no more complications of labor than might be expected in any large series of cases. When the membranes rupture before the onset of labor, they probably do so only when the presenting part is able to descend far enough to exert pressure upon the forewaters. When this occurs, there is little room for prolapse of the cord which can take place only when the presenting part is poorly adapted to the inlet of the pelvis. This concept is confirmed by the fact that there were no cases of prolapse of the cord among the 636 patients with premature rupture of the membranes.

Maternal Morbidity

The maternal morbidity rate for the entire series of 4,806 cases was 7.3 per cent. The maternal morbidity rate for the 636 patients with premature rupture of the membranes was 5.1 per cent indicating that premature rupture of the membranes does not result in increased morbidity. This is even more evident when the causes for maternal morbidity are analyzed.

TABLE V. CAUSES OF MATERNAL MORBIDITY

Pyelitis	9
Cystitis	1
Retained secundines	1
Endometritis	7
Septicemia	1
Infected perineum	1
Upper respiratory infection	1
Aspiration pneumonia	1
Postoperative reactions	3
Unknown	8
	33

Pyelitis, cystitis and respiratory infections cannot be associated with premature rupture of the membranes allowing a correction of the morbidity rate to 3.3 per cent. This increases the validity of the assumption that premature rupture of the membranes does not cause an increase in maternal morbidity.

TABLE VI. MORBIDITY IN RELATION TO THE LATENT PERIOD

LATENT PERIOD	NO. OF CASES	MORBID	%
0 to 1 hour	117	10	8.5
1 to 6 hours	262	10	3.9
6 to 12 hours	112	5	4.4
12 to 24 hours	77	6	7.9
24 to 48 hours	34	1	3.2
48 to 72 hours	14	0	0.0
Over 72 hours	20	1	5.0
Total	636	33	5.1

As can be seen in Table VI, the maternal morbidity rate was greatest in the group of patients whose membranes had been ruptured less than one hour, and there was no increase in morbidity in relation to the increase of the latent period. Only two of the 68 patients with a latent period of 24 or more hours were morbid; one of these was due to pyelitis, and the other to endometritis. Only one of the 34 patients with a latent period of 48 or more hours was morbid and this was due to pyelitis. The most serious post-partum infection, septicemia, occurred in a patient whose membranes had been ruptured only 1.5 hours before the onset of labor and whose labor had lasted 2 hours and 38 minutes. It is therefore obvious, that with ordinary precautions puerperal infections do not result in spite of the membranes having been ruptured over long periods of time before the onset of labor.

Infant Mortality

TABLE VII

LATENT PERIOD	NO. OF INFANTS	STILLBIRTHS	%	NEONATAL DEATHS	%
0 to 1 hour	119	0		0	
1 to 6 hours	267	1		2	
6 to 12 hours	113	1		3	
12 to 24 hours	78	0		0	
24 to 48 hours	34	3		0	
48 to 72 hours	14	0		0	
Over 72 hours	20	2		2	
Total	645	7	1.10	7	1.10
Total in entire series	4,859	92	1.89	94	1.97

There was a slight decrease in both the stillbirth rate and the neonatal death rate of the cases with premature rupture of the membranes. This difference is probably a significant one, certainly there is no evidence that the life of the infant is jeopardized by a "dry labor."

There was an increase in the number of premature infants in the group of cases with premature rupture of the membranes, 40 in the series of 645 infants. Most of these premature infants were well beyond the viable stage, prematurity being the cause of only 2 infant deaths. There is no evidence in this data to indicate whether premature rupture of the membranes was responsible for the high percentage of premature infants, or whether the membranes ruptured as the initial sign of impending premature labor from some other cause.

Management

It is evident from the above statistical review that the best management of premature rupture of the membranes consists primarily of waiting for the patient to go into labor, difficulties arising only when "meddlesome obstetrics" is initiated. When there is conclusive evidence that the membranes have ruptured, it is best to hospitalize the patient in order that she may be kept under aseptic conditions and constant observation. It is open to question whether this is necessary with intelligent patients since a large number included in this series remained at home and carried on their domestic activities for varying periods of time without bad results. It seems probable that patients are safe from infection unless there is the introduction of some nonsterile object into the lower genital tract.

When the patient is near term, medical induction consisting of castor oil and/or an oxytocic drug may be initiated. Even this is not indicated except for the doubtful reasons of economics or convenience.

Since premature rupture of the membranes should not be considered a complication of late pregnancy, the management of this condition is a relatively simple one.

Conclusions

1. Spontaneous premature rupture of the membranes shortens the duration of the first and second stages of labor.

2. There is no increase in the incidence of operative deliveries.

3. Premature rupture of the membranes usually takes place when the feto-pelvic relationship is favorable enough for the presenting part to enter the pelvis early and easily.

4. There is no increase in the maternal morbidity rate, even in those cases with ruptured membranes for long periods of time before the onset of labor.

5. Premature rupture of the membranes does not jeopardize the life of the infant.

6. Management of premature rupture of the membranes consists of maintaining aseptic precautions and, either inducing labor if the patient is near term, or waiting for the patient to go into labor spontaneously.

I wish to thank the members of the staffs of the Philadelphia Lying-in and the Methodist Hospitals for the privilege of using the records of their private patients which have been included in this paper.

3400 QUEEN LANE

Discussion

DR. ROY MOHLER.—Dr. Bishop's presentation has shown how frequently premature rupture of the membranes occurs in obstetric practice. The incidence of 13.2 per cent which he has stated is probably lower than the absolute incidence since the observation of premature rupture of the membranes was based entirely upon simple clinical evidence. Why premature rupture of the membranes occurs so often has not been explained satisfactorily, but it is an incident in pregnancy which is very important, and until very recently was cited as a definite cause for dystocia.

This presentation has shown that the mean length of labor was shorter in the patients who ruptured their membranes before labor began, than the stated standards for the length of labor and, that the incidences of sepsis and injury to the fetus were not increased because of the incident. These observations are very important, and tend to controvert a generally accepted impression that the early rupture of the membranes was an unfortunate event which would likely increase the normal hazard of labor for the mother and child.

In the past decade, most of us have begun to sense from our experience with the use of artificial rupture of the membranes as a means of inducing labor in selected cases, that it was innocuous, and that the dangers previously ascribed to the incidence were probably mistaken concepts. We know now from this report and other recent observations, that rupture of the membranes does not inhibit the progress of normal labor, and in many circumstances, that it actually facilitates labor. Dr. Bishop's statistical report actually confirms the clinical impression that labor can often be facilitated by artificial rupture of the membranes at certain periods during the progress of normal labor.

I think the facts which have been stated in this presentation are generally appreciated by those who are active and observing in obstetric work. There has been so much adverse sentiment developed against the phenomenon known as premature rupture of membranes, both in the literature and textbooks, that much data will have to be collected and reported before the correct concept will be generally accepted.

DR. CHARLES A. BEHNEY.—Dr. Joseph MacFarland once remarked that it is better to be uninformed than to know something that is not true. This is particularly pertinent with regard to the teaching in textbooks and classrooms regarding premature rupture of the membranes. It has been demonstrated repeatedly by Plass and others that premature rupture of the membranes (dry labor) per se does not increase the duration of labor. Premature rupture of the membranes is usually found to occur more frequently when there is an abnormal presentation, or in connection with disproportion, so that if the cases of premature ruptured membranes are compared with those in which the membranes remain intact until shortly before birth, the former group will usually have longer labors. If, however, the patients with normal presentations and prematurely ruptured membranes are compared with those normal presentations in which the membranes are not ruptured prematurely, it will be found that the normal presentations with premature rupture of the membranes are in labor, on an average, a shorter time than those without premature rupture of the membranes. Furthermore, in abnormal presentations the patients with prematurely ruptured membranes deliver sooner, on an average, than the ones in which premature rupture of the membranes has not occurred. Premature rupture of the membranes before engagement of the head, increases the danger of prolapsed cord. Artificial rupture of the membranes after the head is engaged does not predispose to prolapse of the cord.

Dr. Bishop's conclusions are in entire accord with the reports of most of other investigators of this condition. I am convinced that artificial rupture of the membranes in carefully selected cases is good practice. In toxemia, it is an important prophylactic measure.

DR. J. TOLAND.—I must confess that I still carry a slight chip upon my shoulder on account of the incorrect teaching I received on the point of premature rupture of the membranes during my medical-student and intern days. As my experience increased I found, as I am sure have the other members of this Society, that far from being a calamity, that the premature rupture of the membranes in the vast majority of cases was the welcome herald of a short labor and I still begrudge the anxiety that I felt in my early days, on account of previous erroneous teaching.

DR. BISHOP (closing).—First, in answer to Dr. Vaux. Although some of the patients do get into trouble, I probably was fortunate in my series. I know that in other series, cases of prolapse of the cord have been reported, but most of these followed artificial rupture rather than spontaneous rupture. I feel that spontaneous rupture is a naturally selective procedure. The presenting part is probably fitting well into the pelvis and the labor will probably proceed well. It may be that these patients have done better because they have been more closely watched. That is probably the reason for the decrease in morbidity rate.

Second, in answer to Dr. Sharkey. There have been some cases considered by the maternal mortality committee in which premature rupture of the membranes has been a factor. In 1940, 1941 and 1942, there were 11 such cases. Death in three of these was due to hemorrhage, one to embolism, and three to endocarditis. The endocarditis in each case was the result of heart disease which had pre-existed for a long period of time. The remaining four had septic deaths, but in three "meddlesome obstetrics" was a factor. These patients died, not because they had premature rupture of the membranes, but because it was considered a complication and unwarranted interference was instituted.

THE CLINICAL SIGNIFICANCE OF MIDPLANE PELVIC CONTRACTION*

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THE determination of certain pelvic diameters and the consideration of pelvic morphology is definitely useful in estimating pelvic capacity in its relation to childbirth. In the living individual this information can be readily secured roentgenologically and views made from the superior and from the lateral aspects of the pelvis will enable the observer to study pelvic morphology readily and to determine with essential accuracy the important linear measurements.

There are three portions of the pelvis which are important in such a pelvimetric survey; these are the pelvic inlet, the midpelvic plane and the pelvic outlet. It has been known for a long time that any or all of these portions of the bony pelvis may show a relative diminution in area, but only until comparatively recently has emphasis been made upon the importance of midplane contraction in its relation to labor. Hanson's paper[1] on the transversely contracted midpelvis, published in 1936, is an important landmark.

For the purpose of the present discussion the important pelvic diameters may be reviewed, as follows (see Figs. 1 and 2):

PELVIC INLET	Anteroposterior, transverse, posterior sagittal
MIDPLANE	Anteroposterior, transverse, posterior sagittal
OUTLET	Widest transverse diameter, bituberal†

Some idea of the average ranges for these diameters may be gained from the accompanying table, in which the findings of 500 women have been summarized.[2]

AVERAGE DIAMETER RANGE IN 500 PELVES

	DOLICHOPELLIC	MESATIPELLIC	BRACHYPELLIC
INLET			
Anteroposterior	12.0 to 13.0	11.5 to 12.25	10.5 to 11.5
Transverse	11.5 to 12.25	12.0 to 12.75	12.25 to 13.25
Posterior sagittal	4.5 to 5.5	4.25 to 5.0	4.0 to 4.5
MIDPLANE			
Anteroposterior	12.0 to 13.0	11.75 to 13.0	11.5 to 12.75
Transverse	9.25 to 10.25	10.0 to 10.75	10.0 to 11.0
Posterior sagittal	4.75 to 5.5	4.5 to 5.5	4.5 to 5.5
OUTLET			
Widest transverse	11.3	11.9	12.0

*This study was made possible through grants from the Clinical Research and Teaching Funds of the Yale University School of Medicine.

†We measure the bituberal manually.

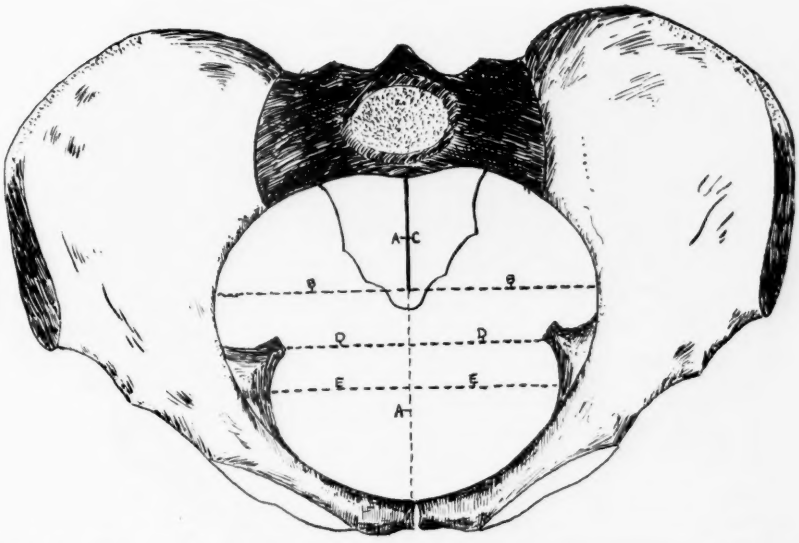

Fig. 1.—The pelvis seen from above. *A*, Anteroposterior diameter of inlet; *B*, transverse diameter of inlet; *C*, posterior sagittal diameter of inlet; *D*, interspinous or transverse diameter of midplane; *E*, widest transverse diameter of outlet.

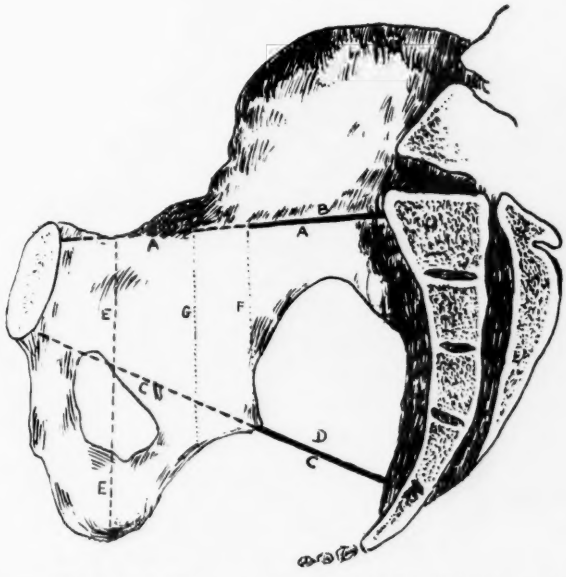

Fig. 2.—Lateral aspect of pelvis. *A*, Anteroposterior diameter of inlet; *B*, posterior sagittal diameter of inlet; *C*, anteroposterior diameter of midplane, *D*, posterior sagittal diameter of midplane.

According to the classification which we have found the most useful, these ranges are divided according to the following pelvic types: Dolichopellic, mesatipellic and brachypellic. The incidence of these pelvic types in a larger group (1,100 women) consecutively studied was 19, 46 and 32 per cent, respectively.

The present paper is concerned with the relative shortening of two midplane dimensions, the interspinous or transverse diameter and the anteroposterior diameter. Our interest in this relative shortening arises from the fact that, in our experience, dystocia at the pelvic midplane resulting from the shortening of these diameters is not uncommon and, when such shortening is present, a knowledge of its degree is of considerable prognostic value. When midplane contraction exists and the pelvic inlet diameters remain within average limits, the fetal head usually shows good engagement, labor proceeds in a natural manner but becomes difficult as the head attempts to pass the midpelvic plane. It is at this level of the pelvis, rather than at a lower point, as Hanson has pointed out, that the greatest difficulty in midforceps delivery is usually encountered.

In the present series of patients showing midplane contraction our particular interest has been in the incidence of operative delivery. It is proper, therefore, that we should consider the meaning of that term as here used. These women, 153 in number, were delivered upon the ward service of the hospital. The series represents delivery at term of 194 pregnancies—153 first and 41 subsequent pregnancies. The operative deliveries represent midforceps, low forceps and cesarean sections. In each case where operative intervention was used, a definite indication was present. In other words, no "prophylactic" or "elective" forceps were performed. In the very few breech cases which occurred, extraction was counted as spontaneous birth unless the forceps were also used in the delivery of the aftercoming head.

In the present study we have chosen to regard a midplane transverse diameter of 10.0 cm. as the lower limit of normal and have, therefore, chosen for this study 153 women whose pelves showed midplane transverse diameters less than this figure. In this group the distribution of pelvic types was as follows:

Dolichopellic	42.4 %
Mesatipellic	41.1 %
Brachypellic	15.6 %
Platypellic	0.65%

The high incidence of the first two types is to be expected, for relative narrowing of the pelvic sidewalls is characteristic of these types. For purposes of analysis, we have divided the series into two groups: Group A, in which the range of the midplane transverse diameter was 9.9 cm. to 9.6 cm. (65 instances); and Group B 9.5 cm. to 8.4 cm. (88 instances). When we consider that in the former group the operative

incidence at delivery was 37.1 per cent and in the latter it was 57.6 per cent, the reason for such divison becomes obvious.

Some of the pelves in this series also showed diminution at the pelvic inlet; in other words, were "small" pelves according to a criterion[2] previously set down, which is:

Dolichopellic type showing an inlet anteroposterior of less than 12.0 cm.
Mesatipellic type showing an inlet anteroposterior of less than 11.5 cm.
Brachypellic type showing an inlet anteroposterior of less than 10.5 cm.

Of the 153 women, 36 possessed pelves which were accordingly "small," and these were distributed according to type:

Dolichopellic	7
Mesatipellic	24
Brachypellic	5

In all instances the contraction at the inlet was not enough to prevent the head from descending to the midplane during labor. The incidence of all operative procedures was 50 per cent and it may be that the influence of the inlet contraction, in addition to that of the midplane, shared the responsibility for such interference.

In discussing midplane pelvic contraction, both transverse and anteroposterior diameters must be considered. When both are relatively shortened, it seems apparent that dystocia must be considered as likely to occur. A knowledge of the average dimensions of the midplane anteroposterior diameter is, therefore, also of importance. In the previous study of 500 women, as shown in the table, these are as follows:

Dolichopellic anteroposterior midplane	12.0 to 13.0 cm.
Mesatipellic anteroposterior midplane	11.75 to 13.0 cm.
Brachypellic anteroposterior midplane	11.5 to 12.75 cm.

In the present series of 153 primiparous women, 75 showed that, in addition to midplane transverse contraction, anteroposterior shortening was also present. These were distributed according to pelvic type as follows:

Dolichopellic type	27
Mesatipellic type	36
Brachypellic type	12

The operative incidence in both A and B groups was 54.6 per cent, but, if we consider those pelves falling in Group B (transverse diameter 9.5 cm. or less), the operative interference rose to 65.0 per cent. In other words, definite transverse shortening plus anteroposterior shortening at this plane markedly increases the incidence of operative intervention. This high incidence is in contrast to 73 pelves (vertex presentation) in which the transverse midplane contraction was not accompanied with anteroposterior shortening. Here the operative incidence was 41.3 per cent for the whole group, and for Group B, 45.2 per cent.

Thirty-two of the 153 women were subsequently delivered on our wards of their second pregnancies, eight of their third child and one

of her third and fourth. Sixteen of these women who were delivered spontaneously of their first infants were also delivered spontaneously in subsequent pregnancies. In the remaining 16 women in whom the first pregnancy was ended by operative intervention, 9 were subsequently delivered spontaneously. The remaining 7 were delivered in the second labor by operative means, but in each instance the midplane transverse was 9.2 cm. or less and in 4 there was present, in addition, definite anteroposterior shortening. Six of these women had pelves which were of the dolichopellic type. In the 9 cases delivered by operative means in the first labor but later spontaneously, all but two showed transverse midplane diameters greater than 9.2 cm. and midplane anteroposterior shortening was present in but four, and in these only to a slight degree. There was one dolichopellic pelvis in this group.

Summary of the Study

Number of pelves studied	153		
Number of labors	153 first, 32 second, 8 third, 1 fourth		
Pelves showing midplane transverse less than 10.0 cm.	153 instances		
Pelves showing midplane transverse 9.9 to 9.6 cm. (Group A)	65 instances		
Pelves showing midplane transverse 9.5 to 8.4 cm. (Group B)	88 instances		
Group A operative incidence	37.1%	Low forceps	16 times
		Midforceps	7 times
Group B operative incidence	57.6%	Low forceps	28 times
		Midforceps	18 times
		Cesarean section	3 times
Pelves showing relative midplane transverse shortening plus inlet anteroposterior shortening	36 instances		
Operative incidence in this group	50.0%		
Pelves showing midplane transverse shortening but no other shortening	73 instances		
Operative incidence	41.3% (Group B alone 45.2%)		
Pelves showing midplane transverse shortening plus midplane anteroposterior shortening	75 instances		
Operative incidence	54.6% (Group B alone 65.0%)		

Group A—32 cases		Group B—43 cases	
Low forceps	8	Low forceps	15
Midforceps	5	Midforceps	10
		Cesarean section	3

In summarizing this experience we wish to observe that midplane pelvic contraction, as indicated by shortening of the transverse diameter, combined or not with shortening of the midplane anteroposterior diameter, is definitely associated with increased operative intervention

during labor. When the midplane transverse diameter is 9.5 cm. or less and the other diameters remain in average limits, according to this study the incidence of intervention was 45.2 per cent. When midplane anteroposterior shortening was also present, operative incidence was 65.0 per cent. In subsequent deliveries, midplane transverse shortening of 9.2 cm. or less with and without accompanying anteroposterior shortening also carries a high incidence of operative necessity. In the patients in this series who were not delivered by operative means, the incidence of prolonged labor in both first and second stages was of frequent occurrence.

Many obstetricians will agree that in certain instances elective cesarean section is to be preferred to the difficult midforceps operation with its frequent attendant severe trauma to both mother and child. It is hoped that by such studies as this, a clearer evaluation of midplane contraction may be secured, so that the conduct of labor may be based less on rule of thumb methods and more on those which offer factual knowledge.

In conclusion we wish to emphasize that, although the knowledge of essentially exact pelvic measurements should never replace sound clinical judgment, which obviously includes the evaluation of the size of the child, character of the labor, etc., the intelligent consideration of such knowledge should form an important aspect of scientific obstetrics.

References

1. Hanson, S.: Am. J. Obst. & Gynec. 32: 385, 1936.
2. Thoms, H.: Am. J. Obst. & Gynec. 42: 957, 1941.

A STUDY OF THE ENDOMETRIAL PATTERN BEFORE AND AFTER TREATMENT FOR AMENORRHEA

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CESSATION of the menses during the reproductive years in the absence of pregnancy, castration, hysterectomy or a masculinizing tumor is a serious and common gynecologic complaint. Diligent study and intensive therapy are often necessary if the reproductive life of the woman is to be salvaged. This report records the observations made upon 9 women whose chief complaint was secondary amenorrhea. The term, secondary amenorrhea, as used in this paper means a cessation of the menses for a period of 5 months or more. A much larger number could be reported if the cases of 2, 3 and 4 months' amenorrhea were included but here the effects of therapy are more difficult to evaluate because of the probability of spontaneous menstruation.

Sex physiology has for its ultimate purpose the procreation of the species. The complex pituitary-ovarian-endometrial system, of which menstruation is but the terminal event, has for its purpose the cyclic maturation of a potentially fertile ovum and the preparation of the endometrium for nidation (Fig. 1). It is believed by many that menstruation per se serves no useful physiologic function. The presence or absence of ovulation is therefore all important physiologically. Accordingly, the 9 amenorrheic patients under consideration here have been divided into 2 groups on the basis of their microscopic endometrial patterns. This provides the best means for determining the presence or absence of ovulation. The finding of a persistent proliferative phase endometrium at successive weekly biopsies indicates a failure of ovulation and therefore a serious pituitary-ovarian defect.[1] The finding of a persistent secretory endometrium at successive biopsies suggests the influence of a persistent corpus luteum.[2] Differentiation of the amenorrheic patients into those with proliferative and those with secretory phase endometriums is essential to correct therapy as will be evident later in this paper. Repeated endometrial biopsies at weekly intervals are necessary to establish the endometrial type. No patient was included in this group unless at least three biopsies taken at approximately weekly intervals were available for study.

Amenorrhea Associated With Proliferative Phase Endometrium

Seven of these 9 patients had a persistent proliferative phase (anovulatory) endometrium. These endometriums varied from a very atrophic type with scarcely any glandular structure (Case 1—Fig. 2), to a marked hyperplasia such as that shown in Case 7 (Fig. 2). Examina-

tion of the endometriums from these 7 amenorrheic patients shows a wide variation of endometrial pattern in this type of amenorrhea. (Fig. 2.) The pattern in any one case, however, is extremely constant. When weekly biopsies were taken on these patients, it was found that there was an amazing persistence of the endometrial pattern in each individual patient. For this reason only one photomicrograph from each patient is shown, this being the biopsy taken just before beginning treatment. In each case this third biopsy was identical with the previous two on that patient.

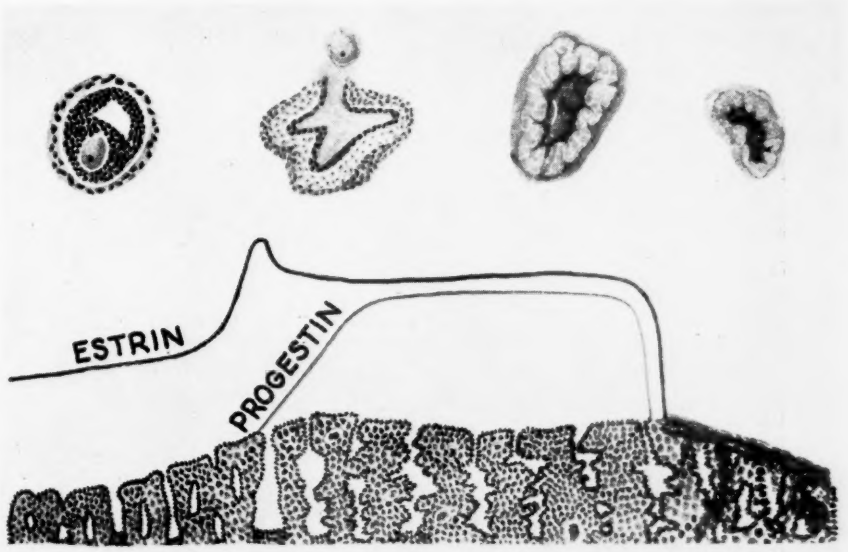
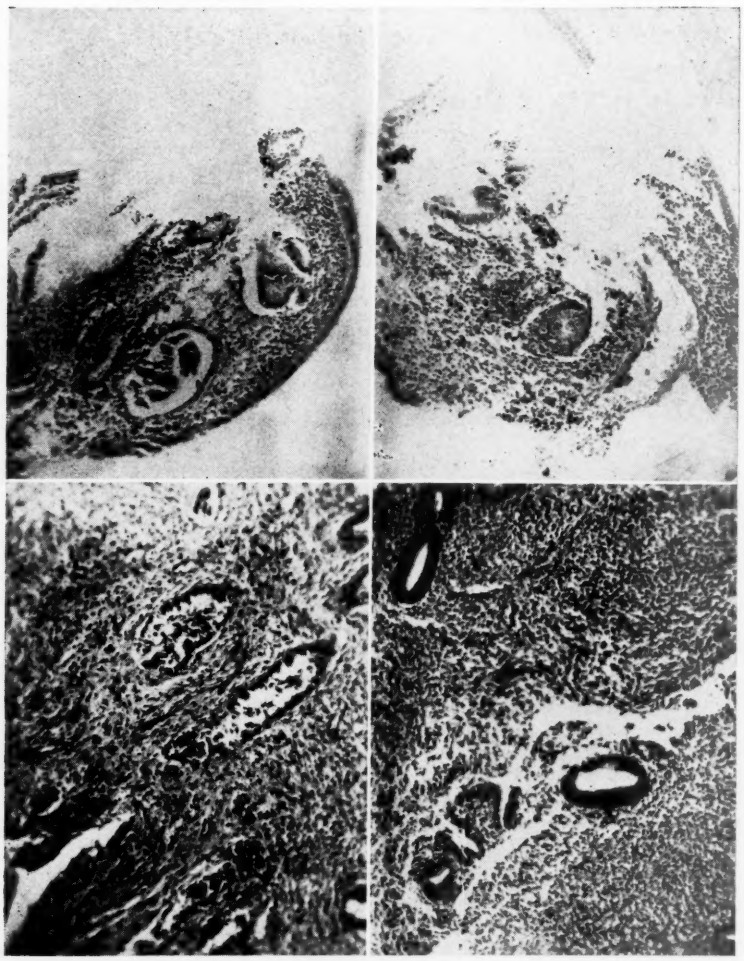


Fig. 1.—Under stimulation of the gonadotropic hormone from the anterior pituitary the Graafian follicle is stimulated to grow and after about two weeks of growth it ruptures extruding the ovum. Estrogen produced by the growing follicle shows the growth or proliferative phase in the endometrium. Under influence of the corpus luteum, the secretory phase of the endometrium is produced with its fuzzy, saw-toothed glands. Sudden atrophy of the corpus luteum about the 26th day of the cycle brings about a sudden estrogen-progesterone withdrawal which provides the bleeding stimulus to the spiral end-arteries of the endometrium.

The pathologic physiology involved in anovular amenorrhea is fairly well understood. It is thought to be the result of a pituitary- ovarian failure, primary or secondary to some systemic disease. Due to insufficient gonadotropic stimulation from the anterior pituitary or to refractivity of the ovary, a Graafian follicle fails to mature and there is no ovulation.[1] No rise and fall in the estrogen level occurs as one finds in the normal cycle; there is no progesterone and so the normal estrogen-progesterone withdrawal from the involuting corpus luteum is absent. (Fig. 1.) Thus, the usual stimulus to the spiral end-arteries of the endometrium is absent and no bleeding occurs. The persistent, unchanging pattern of the endometrium week after week indicates a fixation of the hormone level. Since bleeding usually follows sudden estrogen or progesterone withdrawal, the normal stimulus to menstruation is lacking.

Case 1.

Before Treatment After Treatment



Case 2.

Fig. 2.—*Amenorrhea with proliferative phase endometrium.*

Case 1.—First endometrium after 3 years' amenorrhea, marked atrophy of both the stroma and glandular structure. No change followed treatment. No menstruation. Patient's age, 19.

Case 2.—First endometrium taken from a patient, aged 26, after 11 months' amenorrhea. Note the atrophy of the glandular structure but fairly good stroma. Second biopsy taken at onset of bleeding episode 4 days after completing first course of treatment. No bleeding followed second course of treatment and no menses occurred afterward.

Treatment.—Since the normal stimulus to uterine bleeding is the sudden withdrawal of estrogen-progesterone from a higher level to a lower one (Fig. 1), an attempt was made to simulate this normal physiology and thus induce uterine bleeding.[3] After the patients had been adequately studied by successive biopsies, they were given stilbestrol 5.0 mg. daily at bedtime for 10 nights. On the last 5 days of the stilbestrol therapy, it was supplemented by progesterone 5.0 mg. daily intramuscularly.[3] Following this intensive 10-day therapy, uterine bleeding occurred in 6 of the 7 patients within 4 days. The average duration of the induced menstruation was 3.5 days. One patient (Case 1), who had such marked atrophy of the endometrium, failed to menstruate. In the 6 successful patients, the 10-day course of treatment was repeated on the fifteenth day from the first day of the induced bleeding. Stilbestrol 5.0 mg. was given for 10 days supplemented by progesterone 5.0 mg. on the last 5 days of the 10-day treatment. In other words, the treatment was given from the fifteenth to the twenty-fifth day of the induced cycle. Five of the 6 patients had another episode of uterine bleeding within 15 days after completing the second course of therapy. No further treatment was given. Of the 5 patients in whom a second bleeding phase was induced, all continued to menstruate at fairly regular intervals for periods of 7, 3, 12, 9 and 12 months respectively without further treatment. Of these, 2 lapsed into their original amenorrheic state when treatment stopped, but only after 3 and 9 months of spontaneous menstruation respectively.

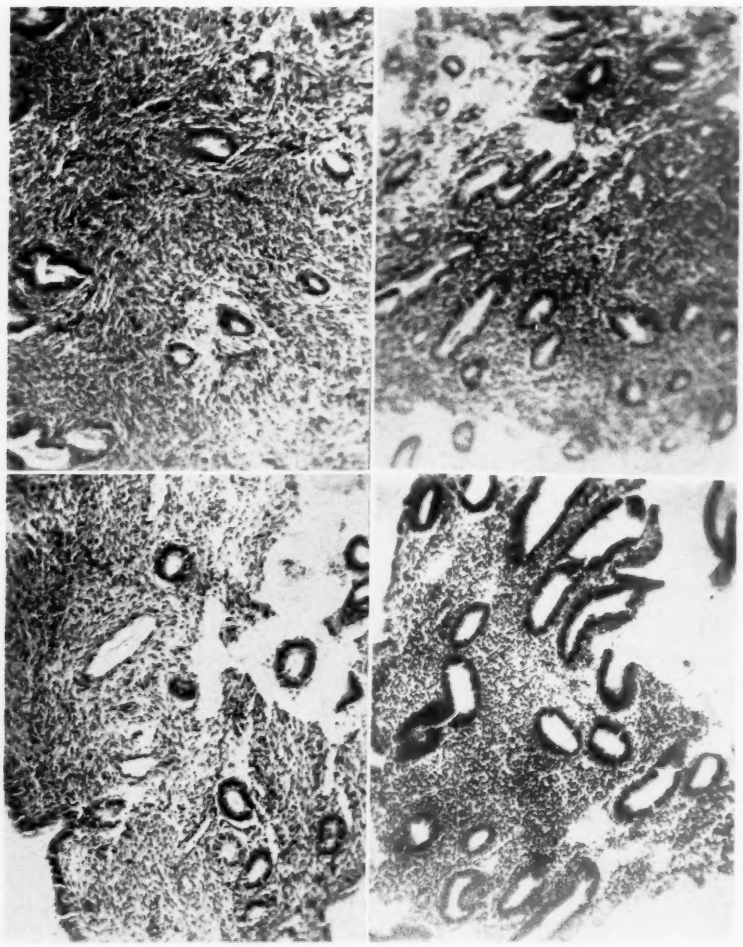
An endometrial biopsy was taken at the onset of the first induced menstruation in the 6 patients. Photomicrographs of these endometriums can be seen in Fig. 2 opposite the endometriums from the same patients prior to treatment. It will be noted that in no case was there a marked alteration in the endometrial pattern as a result of treatment. This lends further evidence to the belief that menstruation is a spiral end-artery phenomenon induced by estrogen-progesterone withdrawal having little relation to the endometrial pattern.

Case 1.—Virgin, aged 19, had 3 scanty menses at the age of 16, amenorrhea for 3 years. She had an infantile uterus with marked atrophy of the endometrium. (Fig. 2.) No bleeding followed the course of treatment described above. Patient has been followed for 2 years and no menstruation has occurred. This amenorrhea may be the result of an endometrial defect not related to any endocrinopathology.

Case 2.—M. L., aged 26, menses always regular, menarche at 17. Amenorrhea of 11 months when first seen. Endometrium moderately atrophic. Stilbestrol-progesterone treatment was followed by scanty menstruation on the fourth day. Second course of treatment followed by no bleeding episode. No menses since. (Fig. 2.)

Case 3.

Before Treatment After Treatment



Case 4.

Fig. 2.—*Amenorrhea with proliferative phase endometrium.*

Case 3.—First endometrium taken on patient, aged 22, after 5 months of amenorrhea which began suddenly. Menstrual cycle had previously been regular. Second endometrium on this patient at onset of bleeding episode 4 days after completing first course of treatment. Cyclic menstruation recurred for 7 months and stopped.

Case 4.—First endometrium taken on a patient, aged 33, whose amenorrhea dated from a difficult delivery complicated by hemorrhage 18 months previously. Second endometrium taken just before bleeding episode following treatment, note that despite the induction of bleeding, there is no demonstrable change in the endometrium. Two months of treatment was followed by cyclic menstruation for 3 months at which time the patient could no longer be traced.

CASE 3.—A. Q., aged 22, nulligravida, married, 3 years' sterility, menses fairly regular until last year, amenorrhea 5 months, persistent proliferative endometrium. Treatment was followed in 4 days by normal 6-day flow. Second course of treatment followed by normal flow and fairly regular menses persisted for 7 months without treatment and then stopped. (Fig. 2.)

CASE 4.—R. L., aged 33, para i, amenorrhea since delivery of stillborn fetus as result of placenta previa 18 months previously. First and second course of treatment followed by normal menstruation which persisted for a period of 3 months at which time the patient disappeared. (Fig. 2.)

CASE 5.—M. C., aged 29, menses always irregular, menarche at 16, amenorrhea since spontaneous abortion with hemorrhage 7 months previously. Normal menstruation followed treatment and a cycle of 35 to 45 days has persisted for 1 year. (Fig. 2).

CASE 6.—R. M., aged 23, normal menarche and normal menstrual cycle until 5 months previously. Menses stopped suddenly, amenorrhea since that time, persistent proliferative endometrium. Normal cyclic menstruation established following treatment described above and this persisted for 9 months without treatment (Fig. 2), at which time she lapsed into her amenorrheic state.

CASE 7.—L. S., aged 21, virgin, menses always irregular, amenorrhea for 5 months, persistent proliferative endometrium, polypoid. Normal cyclic menstruation has persisted for 1 year since treatment. (Fig. 2.)

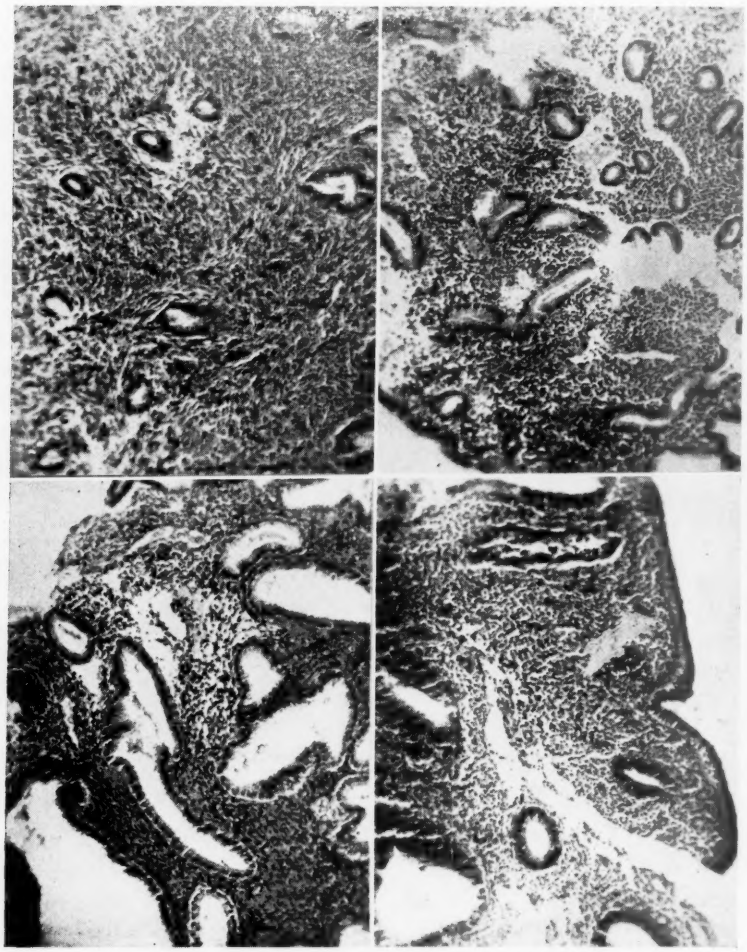
Amenorrhea With Secretory Phase Endometrium

Two of the 9 amenorrheic patients here considered were found to have persistent secretory phase endometriums. (Fig. 3.) The presence of a secretory endometrium indicates a persistent corpus luteum. It has been shown by Corner and others that menstruation in the monkey may be delayed for long periods of time by the administration of large doses of progesterone. The presence of a persistent corpus luteum maintains the progesterone and estrogren level at a fixed point. Since no atrophy of the corpus luteum occurs, there is no estrogen-progesterone withdrawal and the normal stimulus to uterine bleeding is absent. This etiologic factor as a cause of amenorrhea is rarely diagnosed and these patients may go for many years sterile and without the psychic benefit of periodic menstruation.

CASE 8.—D. M., aged 27, nulligravida, menarche age 12, normal 28-day cycle until 14 months previously. Patient had her last menstrual period November, 1941. In January, she consulted an obstetrician who gave her prenatal care until April, 1942. At this time it was discovered that she was not pregnant and various types of chorionic gonadotropins

Case 5.

Before Treatment After Treatment



Case 6.

Fig. 2.—*Amenorrhea with proliferative phase endometrium.*

Case 5.—First endometrium taken on patient, aged 29, whose amenorrhea dated from an abortion with profuse hemorrhage 7 months previously. Normal proliferative phase endometrium. Following two courses of treatment, the endometrium shows some evidence of estrogen stimulation but no progestin influence. Despite little change in the endometrium, the patient had spontaneous but irregular menses which persisted for over a year after treatment.

Case 6.—First endometrium shows early cystic endometrium of a persistent proliferative phase. Taken on patient, aged 23, after 5 months' amenorrhea which occurred suddenly in what had previously been a regular cycle. Second endometrium shows no evidence of stimulation but menstruation followed treatment and has recurred at intervals of 28 to 30 days for 9 months.

were administered irregularly for a period of 6 months. She was seen in January, 1943, with no complaint other than amenorrhea of 14 months' duration. Endometrial biopsy showed persistent secretory phase. There was no pelvic pathology and the ovaries were normal to palpation. Despite a negative pelvis, the diagnosis of persistent corpus luteum was made and a laparotomy performed. At the operating table the ovaries were smooth and normal size, no follicle cysts. Incision deep into the right ovary exposed a healthy, glistening, yellow corpus luteum approximately 1 cm. in diameter. It was excised and menstruation followed on the second day and recurred at 27- to 31-day intervals until the patient became pregnant in August, 1943, after 6 years' sterility. (Fig. 3.)

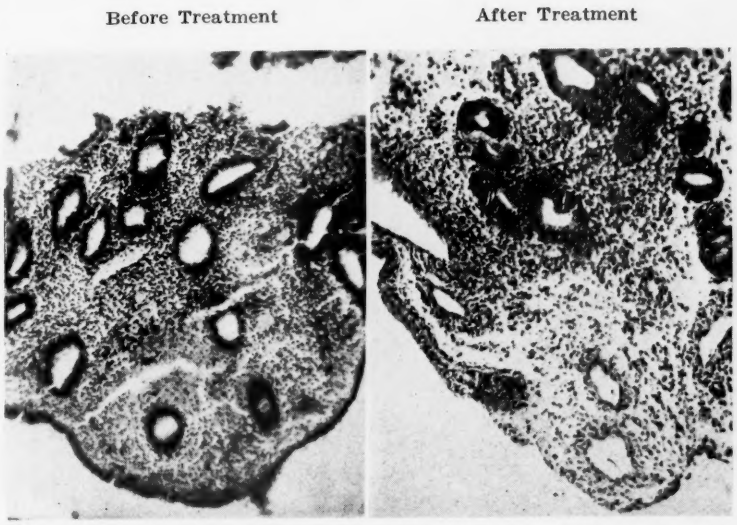


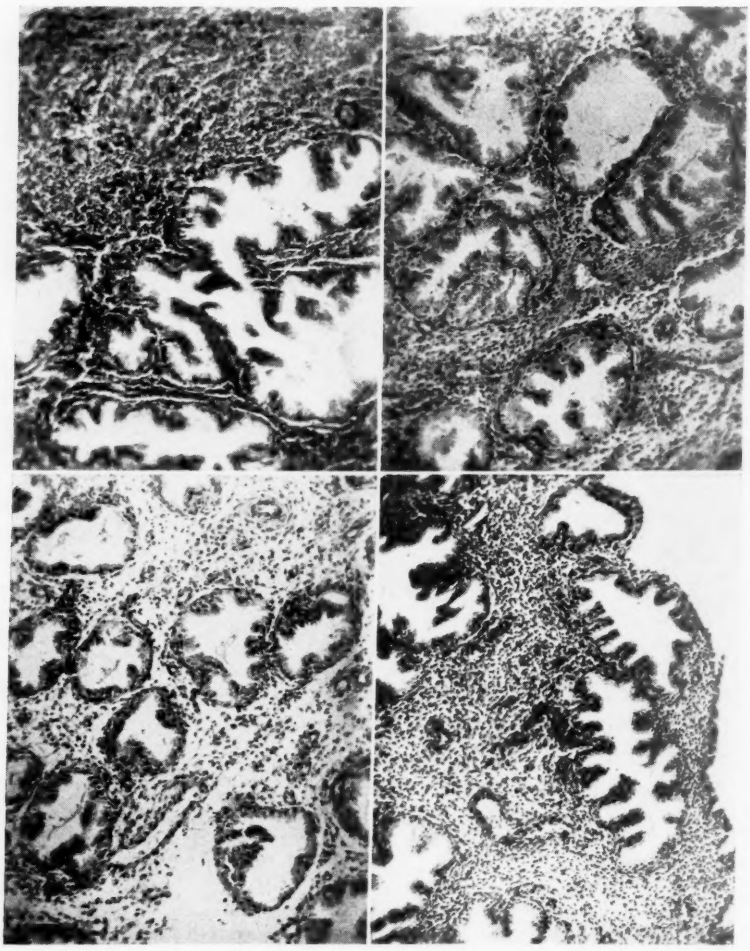
Fig. 2.—*Amenorrhea with proliferative phase endometrium.*

Case 7.—First endometrium taken on patient, aged 21, menses always had been irregular but amenorrhea at the time of biopsy had persisted for 5 months. Polypoid proliferative phase endometrium. Following treatment the endometrium shows a cystic hyperplasia. Menstruation began the first 5 days after completing treatment and has recurred cyclically for over 1 year.

Case 9.—V. C., aged 25, married 2 years with no pregnancies, came under treatment for sterility in September, 1942. Menstrual history always normal. Complete sterility study revealed anovulatory cyclic bleeding as the only sterility factor. No treatment was given but the patient failed to menstruate at the appointed time in December, 1942. She was examined by this author and thought to be pregnant. No symptoms of pregnancy and no weight gain prompted a re-examination in February, 1943. The uterus had not enlarged but the Friedman test was positive. The patient was followed for 2 more months during which time her amenorrhea persisted and the uterus did not enlarge. At this time, a soft, doughy mass in the region of the left ovary estimated to be 9 cm. in diameter could be palpated. Repeated endometrial biopsies

Case 8.

Before Treatment After Treatment



Case 9.

Fig. 3.—*Amenorrhea with secretory phase endometrium.*

Case 8.—Patient, aged 27, menses always regular until onset of amenorrhea 14 months previously. Repeated endometrial biopsies showed a persistent secretory phase such as that seen in the first photomicrograph. This was taken in the ninth month of amenorrhea, many different types of endocrine therapy had been used without success. Following removal of a persistent corpus luteum from the right ovary, menstruation occurred on the second postoperative day. Menstruation recurred at regular intervals and the next biopsy taken at the onset of the patient's third bleeding episode is shown.

Case 9.—Patient, aged 25, developed an amenorrhea of 5 months' duration, while under treatment for sterility. Friedman test was positive but patient was not pregnant. Repeated endometrial biopsies showed a persistent proliferative phase until onset of the amenorrhea when the endometrium assumed the pattern seen in the first photomicrograph. This was taken in the fourth month of amenorrhea. A corpus luteum cyst of the left ovary measuring 6 cm. in diameter was removed, menstruation followed in 3 days. The secretory endometrium seen in the first picture reverted to a normal proliferative one on the fourteenth postoperative day. Normal cyclic menstruation has persisted since that time. The absence of pregnancy was confirmed by curettage at the time of operation and no chorionic villi were found.

at this time revealed a persistent secretory phase endometrium. The patient was operated upon by the author in May, 1943. A corpus luteum cyst of the left ovary about 6 cm. in diameter was removed. Thorough curettage revealed no chorionic villi. (Fig. 3.) The patient menstruated on the third postoperative day and a normal cyclic menstruation has occurred since that time.

Summary

A comprehensive study on 9 patients with a history of amenorrhea persisting for 5 months or more is presented. Endometrial biopsies taken at weekly intervals made it possible to divide these patients into 2 classes as follows:

1. *Amenorrhea With Persistent Proliferative Phase Endometrium.*—Patients with this type of amenorrhea are usually true endocrine problems, their pathologic physiology being a pituitary-ovarian failure with absence of ovulation. The proliferative endometriums vary from the atrophic proliferative type to that of cystic hyperplasia. The endometrial pattern for each individual patient remains amazingly constant. This suggests that the estrogen level in these individuals is a fixed one and in the absence of any cyclic variation of this hormone level, the spiral end-arteries of the endometrium are denied their normal stimulus for bleeding. It is the estrogen-progesterone withdrawal which provides the end-artery stimulus in the normal woman. Satisfactory treatment for this type of amenorrhea is available in the form of stilbestrol 5.0 mg. daily for 10 days supplemented during the last 5 days with progesterone 5.0 mg. Uterine bleeding follows in 3 to 4 days in most cases and the course of treatment is repeated on the fifteenth to twenty-fifth day of this artificially induced cycle. Immediate results were good in that 6 of 7 patients menstruated immediately following treatment and 5 of them continued to menstruate without treatment for variable periods of time. An interesting observation is that despite the induction of bleeding, there occurred little change in the endometrial pattern following treatment. Comparison of the photomicrographs in Fig. 2 shows little difference before treatment and after menstruation had been induced.

2. *Amenorrhea With Persistent Secretory Phase Endometrium.*—A type of amenorrhea rarely diagnosed is that caused by a persistent corpus luteum. Two patients are reported with long periods of amenorrhea and on whom persistent secretory endometriums were obtained. Both patients were originally diagnosed as pregnant and, indeed, one was found to have a positive Friedman test. Both resumed normal menstrual cycles after excision of a small corpus luteum in the right ovary of one, and the removal of a corpus luteum cyst in the left ovary of the other after 14 and 6 months' amenorrhea respectively. Undoubtedly, there are some cases in which a persistent corpus luteum un-

dergoes atrophy spontaneously with re-establishment of the normal cycle. However, those patients with persistent amenorrhea in whom repeated secretory phase endometriums are obtained, a diagnosis of persistent corpus luteum or corpus luteum cyst can be made and the treatment is excision of the corpus luteum.

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GENITAL TUBERCULOSIS IN THE FEMALE

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THE low incidence of genital tuberculosis in the female seldom permits the accumulation of cases in number sufficient to be of significant statistical importance. Only by the continued reporting of smaller series can an adequate literature be built up, and to this end the present report is made. Recent articles[9-11, 14-16] tend to give the impression that the disease commonly involves only one or two of the pelvic structures. This trend is undesirable, since it has been our experience that the disease is usually widespread, and therefore not readily amenable to limited therapeutic measures.

Material

Sixty-two cases seen between January, 1920, and July, 1941 form the basis for this report. In every instance the diagnosis was confirmed by histologic examination, a criterion of selection by which unproved cases are excluded.

The patients ranged in age from 15 to 61, the average being 30 years. Sixty per cent were between 20 and 40 when admitted.

The complaints which brought these patients to the hospital are recorded in Table I. It is evident that none is characteristic of the pelvic disease.

Table I. Admittance Complaint

COMPLAINT	NUMBER OF PATIENTS	PERCENTAGE
Abdominal pain	22	35.4
Sinuses or fistulas	10	16.0
Vaginal bleeding	7	11.3
Back pain	7	11.3
No complaints	3	4.8
Ascites	2	3.2
Abdominal tumor	2	3.2
Amenorrhea	2	3.2
Other	2	3.2
Pruritus vulvae	1	1.6
Urinary symptoms	1	1.6
Sterility	1	1.6
Dysmenorrhea	1	1.6
No statement	1	1.6
	62	99.6

Abdominal pain had led to operative intervention in 12 patients prior to their first admittance to the University of Michigan Hospital.

Since the endometrium and ovaries are commonly involved—as will be shown later—some change in the menses might be expected. This was the case in 58.1 per cent of the patients in this series (Table II).

While these menstrual changes cannot be considered characteristic, it is of interest to point out that hypermenorrhea and irregularity of

TABLE II. MENSTRUAL ABNORMALITIES

TYPE	NUMBER OF PATIENTS	PERCENTAGE
Irregularity	16	25.8
Hypermenorrhea	13	20.9
Amenorrhea	6	9.7
Polymenorrhea	6	9.7
Oligomenorrhea	2	3.2
Postmenopausal bleeding	1	1.6
No change	19	30.6
No information	7	11.3

the menses occurred much more commonly than did amenorrhea, which so frequently has been stressed in connection with pelvic tuberculosis. Table III shows the correlation between ovarian and extragenital tuberculosis in our amenorrheic patients.

TABLE III. RELATIONSHIP OF OVARIAN AND EXTRAGENITAL TUBERCULOSIS TO AMENORRHEA

CASE NUMBER	AGE	OVARIAN TUBERCULOSIS	EXTRAGENITAL TUBERCULOSIS
1	28	0	Generalized
2	19	0	Generalized
3	20	0	? pulmonary
4	22	?*	? pulmonary
5	17	+	None
6	19	?*	Pulmonary

*Ovaries not examined.

It was surprising to note that tuberculosis was present in the ovaries of only one of the four patients in whom the ovaries were examined, and conversely, extragenital tuberculosis was extensive in two of these patients and was probably present in another. One might suspect that the amenorrhea depended more on the character of extragenital tuberculosis than on ovarian involvement. If this supposition were true, a poorer prognosis might be expected in those patients with amenorrhea. However, in our series the survival figures for the amenorrheic cases were practically the same as for the entire series. The long survival of two amenorrheic patients in whom extragenital tuberculosis was absent or questionable (Cases 4 and 5) may have given an abnormally high survival for the group.

Sterility.—The relation between pelvic tuberculosis and sterility is difficult to evaluate. Infertility is said to occur in from 7 per cent to 85 per cent of these cases, being less common in those with myometrial involvement and almost constant when the tubes are affected. Lahmann and Schwartz,[5] considering all types of genital tuberculosis give the incidence of sterility as 26 per cent. In our series there were 46 married patients in the childbearing age. Twenty of these had not been pregnant, making the incidence of "infertility" 43.5 per cent. The word "infertility" is used advisedly since no investigation was made as to other possible causes.

Tuberculosis Elsewhere in the Body.—It is of the utmost importance that tuberculous lesions in other organs and systems should be sought and investigated as to extent and activity, since Peterson showed that these factors play a vital role in determining the outcome of cases surgically treated. Concomitant pulmonary involvement has been reported in from 20 per cent (Lahmann and Schwartz)[5] to 36 per cent (Wetterdall).

In our series 48 per cent had other active foci in addition to the genital lesion. Table 4 shows the organs involved as determined by clinical or postmortem examination.

TABLE IV. ACTIVE EXTRAPELVIC TUBERCULOSIS

SITE	NUMBER OF PATIENTS	PERCENTAGE
Lungs	25	40.3
Abdominal organs	10	16.1
Sinus tracts	4	6.4
Abdominal lymph nodes	3	4.8
Bones and joints	3	4.8
Trachea, larynx, bronchi	2	3.2
Kidneys	1	1.6
Bladder	1	1.6
None found	32	51.6

It is probable that a more thorough search might raise the incidence in these sites. That we are, in recent years searching more carefully may be indicated by the fact that in the first half of the twenty-year period 42 per cent of the patients were found to have extragenital tuberculosis, while in the latter half of the period other foci were noted in 55 per cent.

Analysis of Treatment

Non-Operative Treatment:

Eight patients in this series received nonoperative treatment. Four of this group had far-advanced generalized tuberculosis, and operation was not considered advisable. Management in these cases was purely symptomatic and all died an average of 3.6 months after admittance.

Three patients were treated by bed rest, adequate diet, ultraviolet light, etc., and 2 are alive and well after 10 and 9 years respectively. The third patient in this group died within 8 months after admittance.

One patient with a tuberculous cervix refused treatment, but is alive and denies symptoms, except for amenorrhea, after 20 years. She is now 40 years old.

In these nonoperated cases, the diagnosis was confirmed by examination of biopsy or autopsy material.

Operative Treatment:

Fifty-four patients were treated surgically, the abdominal cavity being opened in 49. The latter can be divided into 3 groups for better comparison of end results with respect to fistula formation and wound infection:

A. Complete pelvic exenteration, with total hysterectomy and bilateral salpingo-oophorectomy. ---------- 13 cases.
B. As in (A) except that the cervix was not removed. -- 13 cases.
C. All other operations, including vaginal hysterectomy, removal of cysts, posterior colpotomy, drainage of abscesses, etc. ---------- 23 cases.

Table V shows the relationship between the type of operation and the frequency of fistulas and wound infections present at the time of discharge.

TABLE V. RELATIONSHIP BETWEEN TYPE OF OPERATION AND WOUND COMPLICATIONS

	GROUP A	GROUP B	GROUP C
Number of cases	13	13	23
Number of wound infections or fistulas	1	4	7
Percentage of cases with wound infection or fistulas	7.7	30.7	30.4

The figures in Table V suggest that perhaps tissue which was not removed at operation had something to do with the wound complications, though the operation may have been incomplete for good technical reasons.

The total incidence of fistulas or wound infection was 24 per cent. This is in marked contrast to the 54 per cent incidence among patients who had been operated on prior to admittance here. Greenberg[3] reported that wound infection occurred in one-third of his 200 cases, and that fistulas resulted in 17 per cent of the drained cases, but in none of those closed without drainage. Lehmann and Schwartz state that 53.3 per cent of their cases developed fistulas. It is interesting to note that we have had only two wound complications since 1930, and none in the 10 patients operated since 1936, although the number of cases has remained quite constant from year to year.

Operative Mortality:

The primary operative mortality was 5.5 per cent. Two patients died on the fourth postoperative day, one of pulmonary embolism, and the other of peritonitis and intestinal obstruction. A third patient died on the nineteenth day of generalized tuberculosis.

Distribution of Pathology:

The incidence of involvement of the various pelvic structures among all the pathologic specimens examined is shown in Table VI.

TABLE VI. DISTRIBUTION OF TUBERCULOSIS IN ENTIRE SERIES

SITE	NUMBER OF CASES SHOWING INVOLVEMENT	PERCENTAGE
Tubes	44	70.9
Parametrium	39	62.9
Endometrium	27	43.5
Ovaries	17	27.4
Cervix	7	11.1
Myometrium	3	4.8
Vulva	1	1.6
Vagina	0	0.0

Since all the genital organs were not available for examination in every case, this table does not represent the true incidence of involvement. There were 13 operative and 5 autopsy cases in which all the internal genitalia were removed and examined. The distribution of tuberculosis for this group is somewhat different, as shown in Table VII.

As would be expected, the incidence of involvement has risen in all the tissues in this group, but of special interest is the increased cervix involvement. Our findings tend to bear out Jameson's[2] statement "... there is no doubt that if the cervix were removed in every hysterectomy and submitted to histological examination, the incidence of cervical tuberculosis would be greatly increased ..." It is the practice of many

TABLE VII. ACTUAL DISTRIBUTION OF PELVIC TUBERCULOSIS

ORGANS AND TISSUES	NUMBER OF CASES	PERCENTAGE
Tubes	17	94.4
Parametrium	12	66.6
Endometrium	11	61.1
Ovaries	7	38.8
Cervix	5	27.7
Myometrium	3	16.6

when removing the uterus to leave the cervix in situ unless it is obviously diseased. There are times when it is unwise to subject the patient to the added risk and time required for complete hysterectomy. However, in view of the frequency of cervical involvement, it would appear advisable to perform a total hysterectomy whenever possible.

Follow Up:

All 62 patients in this series have been carefully followed. Seventeen (25.8 per cent) are dead after an average of 2.3 years. Five died of causes related to pelvic tuberculosis or its extension. The remaining 12 died of causes other than pelvic, the most common being pulmonary and generalized tuberculosis.

Forty-five patients (74.2 per cent) are alive, an average of 10.5 years after their original admittance. Over half of these (57.7 per cent) claim good health. Wound sinuses persist in only 2 patients.

Discussion

It is interesting to note that so few patients gave evidence of tuberculosis elsewhere in the body. There are several possible explanations for this:

A. Tuberculosis may have been present elsewhere, but not discovered.

B. The portal of entry may have been the genital tract, and spread elsewhere may not have occurred. It has been shown by Jameson[2] and others, that in laboratory animals infection of the genitalia can be accomplished by this route. Jameson also cites two human cases in which the evidence strongly suggests that the infection was of the ascending type.

C. The infection may have been hematogenous, and the genital organs the most fertile field for its development, while the primary focus remained silent and undetected.

This leads to consideration as to whether genital tuberculosis is primary or secondary. The literature contains many cases thought to represent primary or secondary tuberculosis. Such reports may have some academic interest, but from a practical standpoint, it is the character and extent of extragenital tuberculosis, and not merely its presence or absence which is important for proper management of the patient.

Since the patients treated surgically and those treated conservatively were not similar in respect to extent and severity of the disease, the better end results in the former group cannot be construed as an indication that operative treatment is always preferable. The difficulty in establishing the diagnosis without operation continues to make evalua-

tion of nonoperative treatment hazardous. However, it seems to be the general opinion[2, 6, 12, 13] that a patient will do better if the diseased tissue is removed by radical operation. Furthermore, Jameson, in reviewing the literature, found a composite salvage rate of 73 per cent for radical operative procedures and 62 per cent for conservative operations. The data in Table V definitely suggest that, at least from the standpoint of wound healing and fistulas, once the abdomen is opened, all the genital organs, including the cervix, should be removed if possible. Tissue conservation does not seem justified.

Summary

1. Data are presented on 62 cases of proved genital tuberculosis admitted to the University of Michigan Hospital during the last 20 years, with follow-up studies on all cases.

2. There were no clinical signs or symptoms pathognomonic of pelvic tuberculosis.

3. Sixty per cent of the patients were in the childbearing age.

4. Forty-three and one-half per cent of the married patients had not conceived.

5. One-half of the patients (51.6 per cent) revealed no evidence of active extragenital tuberculosis.

6. When operative treatment is indicated, all the genital organs including the cervix, should be removed if possible, even though the latter appears normal grossly.

7. Wound complications (infection and fistulas) are much more common after incomplete operations.

8. Seventy-four per cent of the patients in this series are alive an average of 10.5 years after their first admittance.

9. Fifty-four per cent of the survivors claim good health, with no untoward symptoms.

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THE FREQUENCY OF ANOVULATORY MENSTRUATION AS DETERMINED BY ENDOMETRIAL BIOPSY

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CORNER in 1927 was the first to suggest that the anovulatory cycles which he had observed in monkeys might occur in human beings.[1] Earlier investigators had reported that anovulatory bleeding occurred in the monkey, but Corner was the first to have a controlled group of animals with menstrual histories. He found that out of twenty-seven cycles only seven were ovulatory.[2, 3] Later Hartman showed that anovulatory cycles could occur in monkeys at any time in the midst of a series of ovulatory cycles;[4] and Bartelmez,[5] in a review in 1937 cited seventeen satisfactory human cases in which menstruation had occurred at the expected time without either ovary containing a corpus luteum which could be ascribed to the immediately preceding cycle. The endometria, as Corner showed, were nonsecretory in type when anovulatory bleeding occurred, and Robertson, Maddux, and Allen[6] demonstrated that uterine bleeding occurred in castrated monkeys following the withdrawal of injections of female sex hormone.

Anovulatory bleeding may be expected to be most frequent at the menopause and at puberty, when corpora lutea seldom occur and the Graafian follicles persist. These phenomena are correlated with the relative sterility of these periods.[7] The frequency of anovulatory menstruation has been variously estimated. Mazer and Ziserman[8] reported that twenty out of forty-one sterile women showed anovulatory cycles, whereas Tietze[9] found that only 7 per cent of his sterility patients showed anovulatory endometria. Lass and his co-workers[10] reported that in forty-seven lactating women with previously regular menses, 106 (55 per cent) of 194 cycles were anovulatory. Morton and Hayden found only 7 anovulatory cycles in 142 menstrual periods of thirty-three normal, regular, young women.[11]

In our work we desired to determine the frequency of anovulatory menstruation in a group of women with previously regular menstrual periods. For our patients we were able to secure 103 cooperative women from among the female population of the Kankakee State Hospital. All of these women were psychiatric patients; all had regular menstrual periods. Endometrial biopsies were taken in almost all cases twenty days or more following the last menstrual period. In no case was a biopsy taken when the patient had been menstruating longer than forty-

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eight hours. In a few instances we were compelled to take biopsies earlier than twenty days after the preceding period. However, in this latter group, when the microscopic examination of the specimen revealed a nonsecretory endometrium, it was discarded and the biopsy repeated at a later date in the same cycle, or in the next cycle. The biopsies were taken from as high in the uterus as possible, two specimens being taken from the anterior wall, and two from the posterior wall as advised by Kotz and Parker.[14] All of our biopsy specimens were stained with hematoxylin and eosin. In doubtful cases Best's carmine stain for glycogen, and the thionin stain for mucin were used to elucidate the diagnosis.

In the microscopic interpretation of the specimens, the following criteria were used as indicative of the secretory phase:

1. The presence of secretion, glycogen and mucin, within the lumina of the glands; subnuclear vacuolation was not considered to be a sign of early secretion since it has been shown that this may occur in castrated monkeys under estrogen stimulation alone; however, the presence of glycogen in the rest of the cell was taken as a sign of progesterone stimulation;[12, 13]
2. Characteristic tortuosity of the glands, although this was not present in all the specimens diagnosed as being in the secretory phase;
3. Stroma abundant, particularly in the compacta, with relatively large round cells containing a fairly abundant cytoplasm, and with increasing vascularity and edema.

Since it is likely that some of our biopsies did not include a section of the entire endometrium and were mainly compacta, we relied upon the first and third criteria mainly, although in practically every section of secretory endometrium there was some degree of tortuosity of the glands.

Results

We obtained 261 satisfactory biopsies from 103 women. The pertinent information regarding these patients with anovulation and the results of the microscopic examinations are found in Table I. It will be seen that there are 67 women from whom 3 endometrial biopsies each were obtained. Not all of these, however, are from consecutive periods, since at certain times a previously cooperative patient will refuse to submit to examination only to reverse her attitude completely at a later date. There are also 24 patients with 2 biopsies each, and 13 with 1 biopsy each.

Of the 261 specimens only 14 were found to be nonsecretory, giving a percentage of 5.36. (Although various degrees of endometrial development were noted, we have simply classified our findings as either secretory or nonsecretory.) These 14 anovulatory cycles occurred in 9 or 8.67 per cent of the patients. Two patients showed 3 successive nonsecretory endometria. There was 1 patient with 2 anovulatory cycles out of 3; and 6 patients, of whom 5 had 3 biopsies, and one 2 biopsies,

TABLE I

TOTAL NUMBER BIOPSIES	261	TOTAL NUMBER PATIENTS	103
ANOVULATORY ENDOMETRIA	14	PATIENTS WITH ANOVULATORY CYCLES	9
INCIDENCE	5.36%	INCIDENCE	8.67%

DATA OF PATIENTS SHOWING ANOVULATORY CYCLES

PT. NO.	NAME	GR.	AGE	MENTAL DIAGNOSIS	MENSES	L. M. P.	BIOPSY DATE	MICROSCOPIC DIAG.
9	C., M.	ij	40	Dem. precox hebephrenic type	2d. C.	1. 2/16/41 2. 2/17/41 3. 3/26/41	1. 2/11/41 2. 3/ 5/41 3. 3/27/41	1. Nonsecretory 2. Secretory 3. Secretory
11	C., M.	0	25	Without psychosis Mental deficiency	4d. Mild D.	1. 2/ 5/41 2. 3/ 3/41 3. 3/28/41	1. 3/ 3/41 2. 3/24/41 3. 4/21/41	1. Nonsecretory 2. Nonsecretory 3. Nonsecretory
20	F., N.	ij	35	Dem. precox hebephrenic type	?	1. 2/16/41 2. 3/22/41 3. 4/16/41	1. 3/ 4/41 2. 4/14/41 3. 5/ 5/41	1. Secretory 2. Secretory 3. Nonsecretory
22	G., E.	0	28	Dem. precox hebephrenic type	7d. Neg.	1. 12/16/41 2. 1/20/41 3. 2/26/41	1. 1/11/41 2. 2/25/41 3. 3/20/41	1. Secretory 2. Nonsecretory 3. Secretory
38	K., L.	ij	40	Dem. precox catatonic type	3d. Neg.	1. 2/23/41 2. 2/23/41 3. 4/19/41	1. 2/25/41 2. 3/18/41 3. 4/21/41	1. Secertory 2. Secretory 3. Nonsecretory
55	S., G.	ij	43	Dem. precox hebephrenic type	5d. Scoliosis	1. 1/15/41 2. 3/24/41 3. 4/16/41	1. 2/24/41 2. 4/14/41 3. 5/ 8/41	1. Nonsecretory 2. Secretory 3. Secretory
57	S., P.	ij	36	Dem. precox hebephrenic type	4d. Neg.	1. 2/ 5/41 2. 3/ 1/41 3. 3/25/41	1. 2/25/41 2. 3/22/41 3. 4/14/41	1. Nonsecretory 2. Nonsecretory 3. Nonsecretory
67	W., P.	0	46	Dem. precox hebephrenic type	4-5d.	1. 12/15/41 2. 2/12/41 3. 3/13/41	1. 1/11/41 2. 3/10/41 3. 4/ 4/41	1. Secretory 2. Nonsecretory 3. Nonsecretory
77	M., E.	0	33	Dem. precox simple type	?	1. 3/17/41 2. 4/ 7/41	1. 4/ 7/41 2. 5/ 5/41	1. Secretory 2. Nonsecretory

which each showed one anovulatory cycle. Of the 9 patients showing anovulatory cycles, 4 were nulliparous, and 5 had borne children. Three of the nullipara were under 40 years of age; 2 of the parous women were under 40 years; 1 nullipara and 3 parous women were past 40 years of age. (Table II.)

TABLE II. PATIENTS SHOWING ANOVULATORY CYCLES GROUPED ACCORDING TO AGE AND PARITY

PARITY	UNDER 40 YEARS OF AGE	40 YEARS OF AGE AND OLDER
Nulliparous	3	1
Parous	2	3

The 2 patients with the 3 successive nonsecretory periods were below 40 years of age. The first was 25 years old, a nullipara with regular menses, and completely normal physically. Her mental diagnosis was "Psychosis With Mental Deficiency." The second patient was a 36-year-old para ij with regular menses, physically normal with the diagnosis of dementia praecox. The patient with 2 successive anovulatory periods was 46 years old and nulliparous, suffering from dementia praecox, and physically normal. The remaining 6 patients were all patients with dementia praecox with no physical findings. The first was 40 years of age, a para ij; the second, 35 years of age and also a para ij; the third was a 28-year-old nullipara; the fourth a 40-year-old para ij; the fifth a 43-year-old para ij; and the sixth patient was a 33-year-old nullipara.

From our results it does not appear that parity affects the incidence of anovulation to any significant extent in women who are menstruating regularly. (Table II.) Of 46 nulliparous women, there were 4 who showed one or more anovulatory cycles, giving an incidence of 8.7 per cent; there were 57 parous women, 5 of whom had anovulatory cycles giving an incidence of 8.77 per cent. (Table III.)

TABLE III. GENERAL INCIDENCE OF ANOVULATION ACCORDING TO PARITY

PARITY	TOTAL	NUMBER WITH ANOVULATION	PER CENT
Nulliparous	46	4	8.7
Parous	57	5	8.77

Age would seem to influence the frequency of anovulatory menstruation. Of 36 nulliparous women under 40 years of age, 3 had nonsecretory endometria resulting in an incidence of 8.3 per cent; 2 parous women under 40 years of age were found to have anovulatory cycles out of a group of 29, giving an incidence of 6.89 per cent; 10 per cent of the nulliparous patients and 10.7 per cent of the parous patients, over 40 years of age, had anovulatory cycles. (Tables IV and V.)

TABLE IV. INCIDENCE OF ANOVULATION IN NULLIPARA ACCORDING TO AGE

AGE GROUP	TOTAL	NUMBER WITH ANOVULATION	PER CENT
Under 40 years of age	36	3	8.3
40 years of age and older	10	1	10.0

TABLE V. INCIDENCE OF ANOVULATION IN PAROUS WOMEN ACCORDING TO AGE

AGE GROUP	TOTAL	NUMBER WITH ANOVULATION	PER CENT
Under 40 years of age	29	2	6.89
40 years of age and older	28	3	10.7

Comment

Our results show that anovulatory menstruation is relatively an infrequent occurrence in regularly menstruating women. In women whose menses are irregular, the frequency would probably be higher. Parity is apparently of little significance; but age is a factor, there being a definite increase in the percentage of anovulatory cycles in women past 40 years of age. If a larger group of women was studied, it might be possible to show a definite percentile increase of anovulatory bleeding in women past 40 years of age with each successive year of life until the menopause was completed. There is another factor which we must consider, namely, that our patients are all psychotic women. Of the 9 women who menstruated without ovulating, 8 were schizophrenics, and 1 was a psychotic with mental deficiency. It is well known that schizophrenic patients often cease menstruating for variable periods of time after arriving at an institution; and also that occasionally shock therapy will halt menses. It is also possible that other disturbances may be more frequent in schizophrenics than other types of patients. Without intending to imply any particular type of personality trend, we note, however, that our incidence of 14 anovulatory cycles in 261 menstrual periods compares quite closely with Morton and Hayden's incidence of 7 anovulatory cycles in 142 menstrual periods occurring in 33 normal, regular, young women. Our incidence is 5.36 per cent; theirs is 4.9 per cent. It would have been most interesting to see the effect of gonadotropic hormone upon the endometria of the patients with successive anovulatory cycles, but we were not in the position to carry out this work.

Summary

1. Two hundred and sixty-one endometrial biopsies were taken the last one-third of the menstrual cycle from 103 patients in a mental hospital.

2. Fourteen anovulatory cycles were found in 9 patients. Two patients showed successive anovulatory cycles; seven patients showed both anovulatory and ovulatory cycles.

3. Parity was not found to be a factor, but women past 40 years of age were seen to show a higher incidence of anovulatory menstruation—7.69 per cent as compared to 10.52 per cent.

4. In this group of patients the incidence of anovulatory cycles was 5.36 per cent. The patient incidence was 8.7 per cent.

5. While all the women in this group are psychotic patients, the incidence of anovulatory menstruation in them compares quite closely with that found in normal, healthy women.

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ANALGESIA AND ANESTHESIA FOR OBSTETRICS, INHALATION METHODS*

W. Allen Conroy, Capt., M.C., A. U. S., Chicago, Ill.

THE problems of pain relief in labor by inhalation methods have been obscured many times by the emphasis usually placed on actual drugs and apparatus. It would seem more fruitful to consider what distresses and disturbances that delivery causes mother and fetus, and what degree of narcosis will decrease or eliminate these undesirable phases of an otherwise physiologic process. With these in mind, one could then marshal drugs, methods and skills to reach the desired effects.

The average primipara of these civilized days is unfortunately encouraged in her fear of an unknown experience, by the careless use of the word "pains" by her friends, mother and doctor. She does experience "labor" in its simplest meaning, but unlike her primitive sister, her work is attended by varying degrees of real pain. This distress must not be confused with the underlying contractions of the uterus. Means are in existence to eliminate the pain without markedly affecting the uterine contractions, just as pain in any muscle may be alleviated by drugs, and without loss of consciousness.

The first step, then will be to divorce her from the fallacious and harmful idea that she must be relieved of either consciousness or memory of the birth process in order to undergo it in any degree of comfort. Not till she understands that there can be consciousness and memory of labor without distress, will we eliminate some of the hazards of overuse of drugs. Too much narcosis, whether from nonvolatile or volatile agents, leads to fetal respiratory embarrassment, and to weakening of the uterine contractions. We may use *light hypnosis* with nonvolatile drugs like the barbiturates, scopolamine and paraldehyde. In quite moderate dosage, these induce a state of mental relaxation which enables us to gain the apprehensive mother's confidence. We must, if possible, convince her that freedom from pain is obtainable while she consciously assists in the "work" that her uterus does. Even where we later fail to achieve analgesia, we may help her tolerate some pain if she has the knowledge that possible harm to her baby is being avoided. The term analgesia is literally used here, not as an improper substitute for the word amnesia. A patient who is in a deep sleep, and is aroused to wild activity by pain cannot be said to be freed of pain. To call this effect analgesia is misleading to ourselves, because safe doses of barbiturates and similar drugs are not analgesic, that is, they do not eliminate pain.

*Read at a meeting of the Chicago Gynecological Society, Oct. 15, 1943.

Having obtained the mother's confidence before her labor contractions have acquired any element of intolerable pain, we must next watch for the degree and character of what true pain does accompany the individual contractions as their amplitude increases. During the first stage and early second stage, the tolerance to pain may be greater than normal, due to the light hypnosis already mentioned, and some will be willing to fortify it by small doses of opiates. If the pain factor increases rapidly in severity, we must turn quickly to safer methods before confidence in us is lost.

It is excellent practice to observe the rapidity of onset, severity, and duration of the pain factor of each contraction, as soon as labor becomes painful enough to require stronger measures. (See Fig. 1.) A hand on the uterus, and the sound of the patient's breathing and her outeries will tell us quickly whether pain comes early or late in the contraction, how severe it is, and how persistent. Since for each subject, the pain element will usually parallel the nature of the uterine contraction, it suffices to make a mental graph of contraction alone.

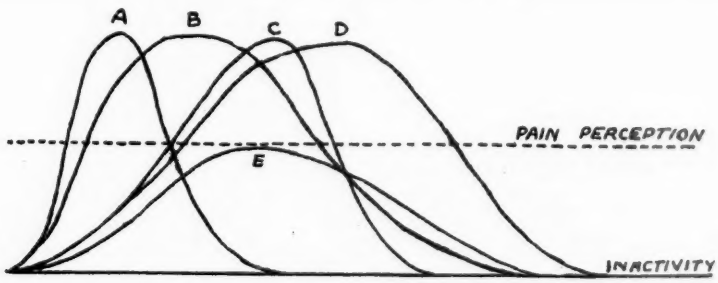

Fig. 1.—Types of contraction pain. *A*, Early, brief perception of pain; *B*, early, prolonged perception of pain; *C*, late, brief pain perception; *D*, late, prolonged pain perception; *E*, pain-free contraction.

Regardless of the inhalation agent used, the principle is the same. We must counteract the pain as rapidly as it builds up, without serious interference to the uterine contraction or hazard to the fetus. If the mother experiences severe pain almost simultaneously with the onset of the contraction, our efforts must be vigorous and swift. If the pain appears late, we content ourselves with the administration of oxygen till pain does appear. If pain is severe or persistent, we are taxed to provide enough pain relief to keep the mother from panicky ineffectuality.

For obstetrical analgesia, nitrous oxide remains our best weapon. Even the tyro will obtain fair results, and with safety, if the color of the patient is kept reasonably pink for the comparatively short time of each contraction, and if overoxygenation is achieved immediately after each contraction. Nitrous oxide may give the desired results with as low a concentration as 50 per cent where the pain element is minor, and may be used in its pure form for the brief and violently

painful contractions occasionally seen. (The lungs and tissues do have a small oxygen reserve.) When commencing to use nitrous oxide, it is wise to give it liberally, even to complete anesthesia, during one or two contractions, to fortify the patient's confidence in our ability to spare her distress. Using our mental graph of the character of pain, we then modify the gas mixture for each subsequent contraction.

If the peak of pain is reached early, the mother is instructed not to delay in asking for the gas, the instant she feels the uterus begin to contract. Better still, if the anesthetist is closely observing the abdomen manually, the first hardening of the uterus is a warning to start administration immediately. With the breathing bag already full with 70 per cent to 100 per cent nitrous oxide, and the valves and gas flow arranged so that all of each expiration is spilled into the outside air, the face piece is applied and the patient instructed to take two maximal inhalations as quickly as she is able. This gives a rapid displacement of the inert nitrogen from the lungs and achieves an analgesic level of the nitrous oxide before the contraction reaches its peak. As the second breath is being taken, the woman is instructed to hold that breath, and strain as if at stool. She will do this effectively once she is confident such activity will be relatively painless. If we know from previous observation that the contraction is short-lived, the breathing bag may be flushed now with pure oxygen. If it is going to be prolongedly painful, the gas is reduced to a level of 85 per cent or less, so that subsequent inhalations will be carrying in adequate oxygen.

Where the onset of pain perception is preceded by a period of painless contraction, three or even four rapid, full breaths of 70 per cent to 90 per cent nitrous oxide will be effective and safe. The longer time will allow for more complete flushing out of the inert nitrogen, but over such a period, the oxygen reserves would be depleted, hence the need for its addition to the gas. Subsequent gas flows for the expulsion efforts to follow will be adjusted to the anesthetist's mental picture of the curve of pain being experienced.

In all cases, flushing with pure oxygen for several breaths, as the uterus relaxes, is essential, to fortify both the mother's and fetus' tissues for the next contraction, when placental oxygen exchange will be reduced by the narrowing of the uterine sinuses and compression of the cord.

In addition to observation of maternal color, it is wise to have a means for the anesthetist to observe constantly any slowing of the fetal heart rate. A heavy stethoscope bell to be taped over the site of fetal heart sounds, and having tubing long enough to reach to the head of the delivery table has been described[1] for such a purpose. Slowing of the fetal heart, regardless of cause and time, should be the signal to increase the mother's oxygen intake immediately.

The other gaseous anesthetics may be, and are, used in a similar fashion. However, nitrous oxide is pleasant and noninflammable, while

ethylene has an unpleasant odor that may lead to nausea, and is inflammable. Its potency is only slightly more than that of nitrous oxide, so little is gained in oxygenation. Cyclopropane offers possibilities of unlimited oxygenation, and is pleasant, but it too is inflammable, and its very potency makes it easy to "overshoot the mark," producing a diminution in uterine contractions.

Of the volatile liquids, ethyl ether is most commonly used, but all too often either ineffectually or to the point of actual anesthesia, with reduction of uterine contractions. The safety factor is great, and its slowness to take effect may be no drawback where the pain of contraction is slow in developing to intolerable levels. Where pain is explosive, it is almost useless, unless a state of near-anesthesia is maintained constantly. Used this way, an increase in nausea, operative interference and fetal apnea is to be expected. Fetal apnea is rare with nitrous oxide alone, nausea is uncommon, and operative interference minimal.

Chloroform and vinyl ether come closest to duplicating the action of nitrous oxide, but the hazards of their use are many and well known. Liver damage is the most feared, but cardiac effects are more frequent and probably quite as dangerous. Other inhalation agents have not received adequate trial as yet.

When there is need for further analgesia or full anesthesia at the moment of expulsion or extraction of the fetus, nitrous oxide-oxygen alone is usually inadequate. Thorough procaine infiltration of the perineum, or the addition of small amounts of ether to the breathing bag are the safest supplementation.

Summary

The obliteration of the pain element of labor contractions is readily accomplished without loss of the patient's cooperation, and without interference with the strength of contractions, or danger to the fetus. Nitrous oxide, combined with oxygen inhalations and supplemented during expulsion, has been found adequate and safe in the hands of many. It, and the apparatus for its administration are available almost universally now, and personnel who know its use are much more plentiful than for the more complicated procedures frequently advocated.*

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*Papers by Drs. Buxbaum, Fitzgerald, Thomson and Brown, and Mengert follow.

Discussion on Symposium on Obstetrical Anesthesia on the Papers by Drs. Fitzgerald, Mengert, Buxbaum, and Conroy

DR. RALPH A. REIS, MODERATOR

DR. REIS.—What about the second twenty-four hours?

DR. MENGERT.—So far we have not had the courage to do it.

DR. REIS.—I would like to ask Dr. Windle a question with relation to what Dr. Conroy said about the time of cutting the cord.

DR. WINDLE.—We published some papers on that subject in which we made clear the reason for delaying until the placenta descended into the vagina.

DR. REIS.—Do you feel the increase in blood volume makes up for the added asphyxia?

DR. WINDLE.—I do not believe that there is additional asphyxia under normal conditions.

DR. CONROY.—During the time that the infant is lying outside the mother, the placenta still intact and the cord pulsating, it may be useful to increase the oxygen in the infant *via* the mother. If separation has occurred the cord should be cut.

DR. BROWN.—Would you add carbon dioxide to the oxygen?

DR. CONROY.—I feel, that the infant while in the mother, has a physiologic level of carbon dioxide from the mother's blood. It is the lack of oxygen that is going to kill it. If you are moving oxygen in and out of the baby's lungs you will keep the baby alive until its sensitivity to normal stimuli occurs. I will not say I have any objection to the use of carbon dioxide, but I feel in most instances, it is not needed.

DR. WINDLE.—I would like to say a word because a year or two ago I spoke to this Society on the use of carbon dioxide in some experimental animals. I am heartily in accord with what Dr. Conroy has just said. It is an academic question, whether you should use carbon dioxide in oxygen or not up to a certain point. The main thing is to get oxygen into the baby when he needs it. If the nervous system and respiratory center of the baby are depressed by barbiturates and other drugs and if the infant's carbon dioxide level is already very high, only then would the use of carbon dioxide with oxygen be contraindicated.

DR. REIS.—Dr. Mengert, have you ever used caudal anesthetic for cesarean section?

DR. MENGERT.—About four times and it has worked very satisfactorily.

QUESTION: Was it continuous or a single injection?

DR. MENGERT.—Continuous.

DR. REIS.—What is your opinion Dr. Huber?

DR. CARL HUBER, Indianapolis, Ind.—We have been using caudal anesthesia in Indianapolis since 1940. We have accumulated about 100 cases of delivery through the birth canal with caudal with results very comparable to those described. In that group, we did not notice the blood pressure drop that Dr. Mengert mentioned as occurring quite frequently. After this experience, we tried caudal anesthesia for cesarean section. The first patient on whom we tried caudal had had two previous sections, the first because of eclampsia, the second one because of the previous section. We followed her completely through the prenatal period in her third pregnancy. She showed no evidence of hypertension, the highest blood pressure being 130/80, with no albumin or other evidence of toxemia. She was given caudal anesthesia with 1.5 per cent metycaine. The injection was preceded by barbiturates. After she had a total injection of 30 c.c. of 1.5 per

cent metycaine, given first as 8 c.c., then 22 c.c., she went into vasomotor collapse, the blood pressure dropping to around 60/40 and staying at that level for a period of approximately three-quarters of an hour in spite of the administration of ephedrine, hypertonic glucose solution and finally plasma. While the blood pressure was at that low level, the fetal heart dropped to 60 beats per minute. When her blood pressure came back to a normal level after this three-quarters of an hour interval, the fetal heart rate returned rapidly to its previous level. We postponed section for 24 hours and it was then performed under general anesthesia. The baby was delivered and breathed without difficulty. It proved, however, not to be a normal baby. The infant was hospitalized for six weeks. It had a few convulsive movements, was stuporous all the time and required gavage feeding. It is now seven months old and is very definitely an abnormal baby. We have no proof, but it is our opinion that this collapse under the caudal anesthesia caused the damage.

We did not feel that this one case should represent the total of our experience, so we tried it again and it worked well. The third section in which we tried caudal anesthesia was in a patient who had had one previous section. She had had a normal prenatal course and it was an elective section at term. We began the caudal anesthesia according to the same technique. About ten minutes after the second injection, for a total of 30 c.c. of 1.5 per cent metycaine, she also went into collapse which was less severe and less prolonged than our first case. She, too, responded to ephedrine. The fetal heart tones dropped to around 50 to 60 per minute and stayed at that level for a period of 15 minutes. We went ahead with the caudal when she responded and injected more metycaine without further reaction and continued the cesarean section. The baby made one or two respiratory efforts and then we were unable to resuscitate it.

We, of course, cannot be sure whether or not the caudal anesthesia was the predisposing factor in these two disastrous instances. They have made us very cautious in the use of caudal anesthesia for section. We wonder if there might be something different in the response of the vascular system in a patient who is not having uterine contractions, and if the danger of vasomotor collapse is not greater than in a patient in active labor. We have done in all five sections, the two described being disastrous as far as the babies were concerned. I would like to ask Dr. Mengert if he has noticed any effect on the fetal heart rate in cases where the mother's blood pressure drops.

DR. MENGERT.—It was a mistake for me to say all four of our sections were done under continuous caudal. One case was an elective cesarean section, in which the patient received 50 c.c. of 2 per cent metycaine. We had no difficulty with the mother or baby in our four sections. The first was an especially interesting one because it occurred in an older patient with a diagonal conjugate of 10.5 Gm. and a disproportion which ordinarily would not be considered insurmountable. The patient was given caudal anesthesia and the resident actually attempted to do a high forceps, but had the good judgment to desist. After two hours of second stage with the membranes ruptured and attempted forceps, a successful section was done. That is why we feel that caudal anesthesia is contraindicated if there is any degree of dystocia which might ordinarily be overcome.

DR. REIS.—In Dr. Huber's case do you think there was any connection between the condition of the infant and the caudal anesthesia?

DR. WINDLE.—I do not think so.

DR. FITZGERALD.—We have done sections under caudal anesthesia and we have not had that particular experience.

DR. BROWN.—We have done eight or nine sections at the Cook County Hospital and in several we did have a fall in blood pressure, but without harm to the

mother or baby. In one case, we had an unusual type of anesthesia to the level of the clavicle, but without any drop in blood pressure or symptoms of respiratory distress.

DR. REIS.—Dr. Brown, will you tell us something about pontocaine *versus* procaine. Do you consider 10 injections in one patient safe?

DR. BROWN.—I think that is carrying things pretty far. That was one reason we sought a longer acting drug than procaine or metycaine. The frequency of injections depends largely on the type of drug, and whether or not epinephrine is employed. Dr. Mengert mentioned using 30 c.c. of 1.5 procaine every 30 to 45 minutes, which involved giving from 400 to 600 mg. of procaine per hour. That is a lot of procaine for the liver to detoxify.

By selecting the drug called pontocaine (Winthrop's brand of U.S.P. tetracaine), we are employing an agent with ten times the potency, and at least double the duration of procaine. On an absolute dosage basis, pontocaine is more toxic than procaine, but when allowance is made for the even greater increase in potency, Nowak found that in cats pontocaine had a corrected toxicity ratio 42 per cent lower than procaine. Is this ratio of 0.58 for pontocaine compared to 1.0 for procaine applicable to the human? Perhaps not, but our clinical experience with pontocaine in spinal and other regional nerve blocks suggests that it is. It conforms to the experience of James of England who uses pontocaine for extensive nerve blocks and infiltration. He regularly obtained three hours of abdominal anesthesia with no toxic effects. We are obtaining three to five hours of anesthesia with our initial dose of pontocaine (1:1,000) in caudal anesthesia. Subsequent injections average a shorter duration, but usually longer than one hour. I would estimate that caudal anesthesia is maintained in pontocaine cases by our technique at the Cook County Hospital with 8 to 20 mg. per hour. Even after multiplying these figures by 10 to convert to the equivalent dosage of procaine, it is evident we are introducing much less drug into the patient than the 400 to 600 mg. per hour of procaine required in Dr. Mengert's technique. The local anesthetic must be absorbed into the circulation and transported to the liver for detoxification. By reducing the total amount of drug, as well as by using a clinically less toxic agent, we feel we are reducing the incidence of toxic systemic reactions. As reported by Dr. Fitzgerald, we have had no major circulatory or respiratory complications. The minor symptoms such as transient headache, precordial distress, and aching in the legs, are phenomena coincidental with, and we feel associated with too forceful an injection of the solution. The major safety factor of any caudal technique should depend on a careful aspiration test, followed by the routine use of a slowly injected test-dose so calculated that it would be a safe intraspinal dose should the needle have penetrated a low-lying subarachnoid space.

We agree with Dr. Buxbaum on the importance of adding a vasoconstrictor to the anesthetic solution as an added safety factor. The addition of suprarenin (1:1,000) in amounts to make a concentration of 1:200,000, contributes definitely to prolongation of the anesthesia from each dose, and makes effective the low (1:1,000) concentration of pontocaine. Without the vasoconstrictor, a higher concentration and more frequent injections would be necessary and, systemic absorption being more rapid, toxic effects would be more likely. Ninety-nine of our 200 cases were performed with pontocaine 0.10 per cent (1:1,000) with suprarenin 1:200,000 (2 minims of 1:1,000 to the ounce) dissolved in physiologic saline.

We agree that continuous caudal anesthesia is limited in its usefulness, effectiveness, and safety, chiefly by the time, skill, and experience of the administrator. Our experience has been that a physician can learn the basic fundamentals of technique in a week, but that a month of training involving 20 or 30 personal administrations affords a more ample competence. No physician should

attempt continuous caudal anesthesia without previous practical experience under expert supervision. Only by adhering to this dictum will this new technique avoid the disrepute that will follow failures and complications, in inexperienced hands.

We should point out while Dr. Huber is here, that he modestly refrained from mentioning that Manalan, of his clinic in Indianapolis, preceded all others historically in the development of a technique for insertion of a ureteral catheter in the caudal canal (early in 1940). In our series at Cook County Hospital, we employed the Hingson safety caudal needle in 90 per cent of the cases, but our use of the 15 gauge Irving needle for introduction of a No. 4 French Bard caudal catheter, confined to 10 per cent of the first 200 cases, will increase in the future.

DR. CONROY.—I think it will be recognized by any one who has done a lot of caudal injections that we are injecting a drug into a highly vascular area and if this is done rapidly, it will bring about circulatory depression. It has been our practice to give a prophylactic vasoconstrictor, like neosynephrine, and when collapse occurs to administer oxygen as well as stimulants to diminish the anoxemia to both mother and baby.

DR. REIS.—Is there not work being done on anesthetic agents with more prolonged action which will not require keeping the needle in place?

DR. CONROY.—Some work is being done at the present time which will give analgesia for five to six hours. The idea was to enable the operator to give a single injection and repeat it perhaps not more than once, using ordinary stock needles which are easier to insert than are the complicated needles.

DR. ALBERT H. LAHMANN, Milwaukee, Wis.—I cannot understand why there are likely to be toxic reactions in caudal anesthesia in cesarean sections. We have reported 58 consecutive sections done under single injection caudal without any toxic reactions and without any additional anesthesia required during the operation. One possible factor is that these patients must be premedicated. Our routine is to give the patient about two hours before the scheduled section 4½ grains of seconal or nembutal, then we inject approximately 75 c.c. of 2 per cent metycaine. Thus far, we have had no untoward reactions. It is true, we may have had a fall in blood pressure which is very transitory. We may have slowing of the fetal heart tones for a short time, but it has never worried us. The thing that has impressed us most is that these babies cry immediately when born. The loss of blood is minimal and the patient goes back to her room in excellent postoperative condition. She takes fluids immediately and is a very cooperative patient.

In 1939 at the County Hospital, Milwaukee, we started work on single injection caudal. In 1942, Dr. Mietus and I reported in *Surgery, Gynecology and Obstetrics* (**74**: 63-68) (Jan.) 450 cases. Since that time, we have given 800 single injections, 78 for multiparas and 722 for primiparas. Complete failure occurred in 4.5 per cent. Failure is due either to technical difficulty in getting into the canal, or sometimes to inability to get anesthesia even when in the canal. Partial anesthesia occurred in 6.7 per cent. This gives a total of 11.2 per cent failure and 88.8 per cent complete success.

Out of the last 450 caudals done at the County Hospital, there were five stillbirths. In breaking this down, one finds that the fetal heart was absent before the injection in 1; prolapse of the cord occurred in 1; an anencephalic monster was found in 1; the fourth was a premature weighing 3 pounds 9 ounces; the fifth was a case of abruptio placentae.

The duration of the anesthesia averaged about one hour and 29 minutes. The quantity of anesthetic in a single injection was about 45 c.c. We occasionally found a drop in blood pressure, which was transitory, and sometimes a little disorientation, but in review, we found that those patients who had disorientation were those patients in whom the barbiturate had not had a chance to take effect.

In these 800 cases we have no local infections. We do not use a wheal because we feel that it obscures the landmarks. I would rather give the patient a whiff of gas for a few minutes while we are inserting the needle.

We have in Wisconsin a new organization called the Wisconsin Society of Obstetricians and Gynecologists, which met this year. The entire meeting was devoted to a practical discussion of what was the status of caudal anesthesia. A committee was appointed to publish a statement in the *State Journal* and then be given to the lay press, telling the public what the obstetricians in the state of Wisconsin thought about continuous caudal. This has been completed. After Dr. Lundy spoke in Milwaukee last Friday and after the committee meeting with Dr. Cunningham of Columbia Hospital, we have gone on record as condemning continuous caudal as a procedure in private practice. Dr. Mengert and Dr. Fitzgerald are working in teaching institutions which are not suffering from loss of man power and nursing care as we are. It is impossible to get away from complications in continuous caudal anesthesia in private practice. Nevertheless, this committee went on record as saying that single injection caudal anesthesia in obstetrics has merit in selected cases. I am sure that three-fourths of the cesarean sections done in the city of Milwaukee are done under single injection caudal. In selected cases, particularly persistent occiput posteriors, breech extractions and perineal floor repairs where a little relaxation is helpful, single injection caudal is a success and I certainly think we are all going to continue to use it in cesarean section.

DR. REIS.—

Dr. Mengert, would you like to comment on single injection caudal?

DR. MENGERT.—We have had no experience with single injection caudal, so I am not competent to comment on it. We used it a few times some years ago and gave it up because it was too cumbersome a procedure to use for routine delivery, and the same result could be obtained with pudendal block. It was not until the continuous method appeared that we revived our interest in caudal anesthesia.

LOCAL ANESTHESIA*

HENRY BUXBAUM, M.D., CHICAGO, ILL.
(From the Chicago Maternity Center)

USUALLY, when one gets up before a critical audience such as this and presents his views relative to a certain type of obstetric analgesia or anesthesia, he almost automatically is placed in a position of attempting to defend his particular method. Fortunately, I was delegated by our moderator to present the case of local anesthesia. I say fortunately, because local anesthesia needs no defense, inasmuch as infiltration as well as regional anesthesia provides anesthesia to the part that is to be operated on rather than to the organism as a whole. Also I respectfully call to your attention that local anesthesia has all the advantages of the other types of anesthesia without any of their disadvantages.

Regarding the margin of safety in the various forms of anesthesia, as a general rule it can be said that the safety of any anesthetic agent increases in direct proportion to the distance with which it is administered from the brain and/or the central nervous system. With this fact in mind, I believe safety of the various forms of anesthesia can be stated in the following sequence:

1. Local infiltration, which is the farthest from the brain.
2. Regional or nerve block, such as parasacral or presacral, and pudendal.
3. Epidural or caudal.
4. Spinal.
5. General or inhalation anesthesia.

The advantages resulting from the employment of regional and local anesthesia are as follows:

1. No anesthetic mortality.
2. No pulmonary complications. Most obstetric patients come to the delivery room with full stomachs, making it almost impossible for even the best anesthetist to give her a smooth anesthetic. Excessive emesis, laryngospasm and aspiration pneumonia are not at all uncommon.
3. Simplicity of administration.
4. No paralytic ileus.
5. No fetal asphyxia.
6. Patient is able to take fluids by mouth during and immediately following the operation.
7. Less local blood loss due to adrenalin.
8. Less tissue trauma with better healing of the wound.

*Presented at a meeting of the Chicago Gynecological Society, October 15, 1943.

9. No interference with the efficiency of the uterine contractions.
10. Perineal floor relaxation with vaginal gaping, and finally,
11. Less postoperative shock.

Among the few disadvantages may be cited:

1. In highly emotional patients, total success with local anesthesia may be impossible and therefore a general anesthetic may have to be supplemented.

2. All surgeons are not temperamentally adapted to use this form of anesthesia, due to a lack of patience, which is a prime requisite for the successful use of local anesthesia, and to the marked tendency toward rapid surgery, which is not at all necessary or even desirable in regional or infiltration anesthesia. Also, every surgeon using local anesthesia must have a wholesome respect for tissue integrity.

3. A minor disadvantage is the accidental breakage of the needle in the tissues, which can be obviated to a great extent by using a long needle and not inserting it up to the hilt.

Regarding the indications for local anesthesia. It has been satisfactorily demonstrated that all major and minor obstetric procedures either by the abdominal or perineal routes can be done under local anesthesia with the possible exception of version. An absolute indication for the use of local anesthesia may be found in patients with upper respiratory infections, pulmonary tuberculosis, asthma and cardiac disease with the omission of the adrenalin. Relative indications are pre-eclamptic toxemia, nephritic toxemia and diabetes. It is also the ideal approach in all cesarean sections with or without sterilization. Here one may use intravenous anesthesia in addition for closure if necessary. In the delivery of a breech presentation, parasacral or pudendal block is especially efficacious due to the relaxation of the pelvic floor and levators. Even if the operator should elect to use inhalation anesthesia, delivery is definitely facilitated by the addition of pudendal block.

Preparation.—According to deTakats, when distilled water is used as a vehicle for a 0.5 or 1 per cent novocain solution, the solution becomes slightly hypotonic, which has a tendency to hemolyze red blood cells and to produce tissue necrosis. Heating of stock solutions also diminish its anesthetic properties. Therefore, we always prepare our anesthetic in normal saline solution just prior to its use. Three minims of adrenalin (1:1,000) are added for each ounce of solution.

Technique.—As a precautionary measure in parasacral or pudendal block anesthesia, one should aspirate before injecting so as to make certain that the point of the needle is not in a blood vessel. In the infiltration method, the solution is deposited in the tissues with the needle in constant motion.

In the infiltration method, the posterior fourchette, lower posterior portion of the vaginal tube, and the ischiorectal fossae are injected. If an episiotomy is to be done, the line of incision is also injected.

In pudendal block, bilateral intradermal wheals are made midway between the tuberosity of the ischium and the anus. Then a 10 to

12 c.c. long, 20 gauge needle is directed to the spine of the ischium with a finger in the vagina or rectum to act as a guide. The point of the needle impinges against the spine, is then disengaged and passed to the dorsal aspect of the spine. Here, 10 to 15 c.c. of the solution are injected, effectively blocking the internal pudic nerve as it passes through the greater sciatic notch immediately posterior to the inferior ischial spine. Then the needle is withdrawn and a shorter needle is substituted, and 5 to 10 c.c. are deposited medial to the inner aspect of the tuberosity of the ischium in a fan-shaped manner, blocking the posterior femoris cutaneous nerve, a branch of the posterior fibers arising from the first and second sacral nerves. This same procedure is repeated on the opposite side.

In the parasacral or presacral technique, a finger is placed in the rectum and the sacrococcygeal joint is palpated. An intradermal wheal is made 2 c.c. from the midline at the level of the sacrococcygeal junction. A 15 c.c., 20 gauge needle is inserted parallel to the midline. The point of the needle feels its way over the edge of the last sacral vertebra and then advances 5 to 7 c.c. until the second sacral foramen is encountered. Then aspirate, and if no blood is drawn, inject 60 to 70 c.c. as the needle is being withdrawn. The angle of the needle is then shifted 15 degrees upward and again advanced parallel to the midline about 10 c.c. until the first sacral foramen is reached. Here, 20 to 30 c.c. of the solution are deposited. This process is now repeated on the opposite side. Lastly, 10 c.c. of the novocain solution are injected between the sacral coccygeal joint and the posterior wall of the rectum, blocking off the anococcygeal plexus.

Regarding the use of local anesthesia in abdominal deliveries, some men elect to use this method routinely, while there are other operators who only resort to local anesthesia when definitely indicated by the physical condition of the mother. Be that as it may, while the percentage of failures is greater in abdominal deliveries than in perineal deliveries, it is by far the safest form of anesthesia we have today at our disposal. The mother usually leaves the table in excellent condition, and is quite elated after hearing her child's first lusty cry. The babies are not lethargic or asphyxiated as they usually are when an inhalation anesthetic is used, but on the contrary cry immediately on their exit from the uterus.

The infiltration method is the most commonly used form of local anesthesia in cesarean sections, although one can block the nerves at the semilunar line if he so desires. Usually the method described by De Lee, and recently modified by Beck, is the method of choice of most obstetric surgeons. Here the three main sites for the deposition of the novocain solution are the skin and subcutaneous tissues, laterally in a semicircle from within, outward to a depth of about 5 c.c. before opening the fascia, and lastly under the loosely attached visceral peritoneum covering the lower uterine segment.

To demonstrate the practicability and safety of regional and infiltration anesthesia, let me briefly cite the statistics of the operative and spontaneous deliveries done at the Chicago Maternity Center with this method of anesthesia. Here, as you are aware, all deliveries are done

in the home under the poorest of physical and sanitary environments. These cases were nearly all done by our resident physicians under the supervision of the attending obstetricians. Up to the present time, from the inception of the institution in 1932, parasacral anesthesia has been utilized in 550 cases, and pudendal block in 2,200 cases, with no maternal or fetal deaths attributable to the anesthetic. There were two cases of abscess formation at the site of puncture. No needle was broken off in the tissues.

If we accept Farr's description of an ideal or successful anesthesia as one in which the operative procedure was completed with no pain or discomfort to the patient, a satisfactory anesthesia as one in which the indicated procedure was completed with only a slight amount of discomfort, and a failure as a case where the local anesthesia had to be abandoned or supplemented with inhalation anesthesia, then our results can be classified as follows:

In the 550 cases where parasacral anesthesia was employed, 314 (57 per cent) were ideal; 203 (37 per cent) were satisfactory; and only 33 (6 per cent) were failures.

In the pudendal block group, 880 cases (40 per cent) were ideal; 1,210 (55 per cent) were satisfactory; and 110 (5 per cent) were failures.

In the parasacral series, all forms of pelvic obstetric surgery were performed with the exception of version. This includes manual and instrumental rotations and difficult midforceps operations. In those cases in which the pudendal block anesthesia was used, the operations were mainly low forceps deliveries, episiotomies and repairs. This was also the procedure in all breech deliveries.

In closing, I wish to submit the following suggestion: Inasmuch as local anesthesia has proved so satisfactory in home obstetrics, it certainly can and should be employed more often in hospital practice, particularly in this day and age, where the anesthetic departments in most hospitals have been so badly depleted.*

8 South Michigan Avenue

*See Discussion on Symposium on Obstetrical Anesthesia, page 85.

CONTINUOUS CAUDAL ANESTHESIA WITH PONTOCAINE: OBSTETRICIAN'S VIEWPOINT*

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CONTINUOUS caudal anesthesia as suggested by Hingson and Edwards[1] for women in labor has been used by many investigators in all parts of the country. Many reports have been published, but both the profession and the public are still far from clear concerning the indications for use of the procedure, or the disadvantages and even dangers associated therewith.

The following report is a preliminary presentation based on the first 200 cases in which repeated caudal injections of pontocaine were used to produce and maintain anesthesia during labor, and covers the five-month period between March 16 and August 26, 1943.

It may be well to note that we speak of *anesthesia* during labor, for this is more than analgesia, for in successful cases the patient, after the introduction of the needle, proceeds through her labor without even the slightest discomfort or awareness of her uterine contractions. It is the only pain relief yet devised that allows a parturient to smile through the hardest uterine contraction and mean it. Nevertheless, certain factors make the obstetrician somewhat cautious in his adoption of the procedure. It is the purpose of this report to present the obstetrician's reaction to the method insofar as the comfort and safety of mother and child are concerned.

Technique

Inspection of the sacral landmarks, an enema, and a soap and water cleansing of the skin over the sacrococcygeal region are preliminary steps. In this series a modified knee-chest position was used in most cases, as this insures accurate identification of the midline. The technique of identification of landmarks, insertion of needle, and evaluation of criteria for accuracy of placement, will not be considered in this paper. Though recommended, a barbiturate was rarely given for premedication. The solutions employed were made up as outlined in Table I:

Technical precautions designed to prevent complications include (1) limitation of concentration, amount, and frequency of injections to the least effective values which will produce and maintain relief of pain; (2) use of a vasoconstrictor in the anesthetic solution; (3) careful aspiration tests; (4) preliminary injection of a safe spinal test-dose con-

*Presented at the Oct. 15, 1943, meeting of the Chicago Gynecological Society. Credit is given to Dr. Bernice Rosen, M.D., and Miss Sedonia Spinka for assistance in the initiation and conduct of this series. Winthrop Chemical Company, Inc., supplied the Pontocaine 250 mg. ampoules and Suprarenin which were used in this series.

TABLE I. PONTOCAINE-SUPRARENIN SOLUTIONS

CONCENTRATION OF PONTOCAINE	PONTOCAINE HCl "NIPHANOID"	SUPRARENIN* 1:1,000	PHYSIOLOGIC SALINE
0.10% (1:1,000)	250 mg.	1.25 c.c.	qs. 250 c.c.
0.15% (1: 666)	250 mg.	0.83 c.c.	qs. 167 c.c.
0.20% (1: 500)	250 mg.	0.63 c.c.	qs. 125 c.c.
0.25% (1: 400)	250 mg.	0.50 c.c.	qs. 100 c.c.

*To make 1:200,000 Suprarenin.

Experience in this series indicates that the 0.10% (1:1,000) pontocaine solution is most satisfactory, and since it is the safest concentration of the four listed, the higher concentrations were rarely used after the first 100 cases. This concentration was used in nearly one-half (99) of all the cases, as listed in Table II.

taining 5 to 10 mg. of pontocaine followed by a delay of 10 minutes; (5) *slow* injection of therapeutic doses; (6) availability of an oxygen machine, a barbiturate, and a 15 gauge spinal puncture needle; (7) rigid asepsis; (8) preference of ureteral catheter technique in cases likely to be prolonged. All patients are kept on their sides most of the time to prevent post-partum backache and needle breakage. One nurse can be taught to care for several caudal patients simultaneously. The Block-Rothstein[2] gravity drip test with saline is employed to identify location of the needle tip when doubt exists. The Irving[3] 15 gauge special B-D caudal needle, preceded by the 18 gauge 5½ inch Irving "inner guide" needle,* has been used in 20 cases of the 200 for introduction of the No. 4 French Bard nylon boilable caudal catheter.† In other cases the Hingson B-D "safety caudal" needle or its predecessor was employed. Other technical details and the reasons for selection of pontocaine will be reported elsewhere.

Distribution of the two hundred cases studied, according to the average duration and total dosage with various dilutions of pontocaine, both with and without suprarenin as vasoconstrictor, are given in Table II.

TABLE II

CASES	% PONTOCAINE IN SALINE	HOURS UNDER CAUDAL				DOSES		AVERAGE AMOUNT IN C.C.
		MAXIMUM HR.	MAXIMUM MIN.	AVERAGE HR.	AVERAGE MIN.	MAXIMUM NO. DOSES	AVERAGE NO. DOSES	
		WITHOUT SUPRARENIN						
20	0.25%	27	30	5	32	15	3.41	80.6
11	0.20%	10	25	5	35	7	4.0	85.5
5	0.15%	12	55	8	23	9	4.8	132.2
		WITH SUPRARENIN 1:200,000						
1	0.25%	1		1		1	1.0	37.0
31	0.20%	17	30	4	33	5	2.5	53.0
20	0.15%	37	15	6	25	14	3.2	79.5
13	0.125%	44	30	8	45	19	4.2	114.5
99	0.10%	38	15	6	10	15	3.0	74.8

Several observers have reported a marked decrease in the period of cervical dilatation. This has not been our experience. In Table III is recorded the elapsed time from administration of the anesthesia to

*Irving catheter introducing needles were supplied by Becton-Dickinson Co., Rutherford, N. J.

†No. 328 caudal catheters were supplied by C. R. Bard, Inc., 79 Madison Avenue, New York, N. Y.

complete dilatation. While such figures are not accurate because rectal examinations are subject to error, nevertheless it is still apparent that in our series cervical dilatation is not accelerated. The further fact that 6 cases without disproportion resulted in prolonged labors (over 24 hours) suggests that the rate of cervical dilatation is not affected.

TABLE III. TIME REQUIRED TO COMPLETE CERVICAL DILATATION

	3 cm.	4 cm.	5 cm.	6 cm.	7 cm.	8 cm.	9 cm.
PRIMIPARAS							
Hours and Minutes	9′ 5″	8′ 27″	6′ 19″	8′ 10″	3′ 58″	3′ 14″	1′ 19″
No. of Cases	7	19	21	13	20	22	13
MULTIPARAS							
Hours and Minutes	8′ 45″	5′ 49″	4′ 4″	2′ 18″	2′	1′ 6″	1′ 50″
No. of Cases	9	16	15	12	5	5	2

Caudal anesthesia results in a complete paralysis of the perineal muscles. These patients cannot empty their bladders. They have no sensation at all when the head is on the perineal floor. They have no abdominal sensation from a level usually just below the umbilicus. Consequently, they have no stimulus to force the fetal head over the perineum. It is true that a proportion of such patients can be taught to use their abdominal muscles so that spontaneous delivery can be accomplished. Nevertheless, the incidence of instrumental deliveries (Table IV) is sharply increased particularly on a service which has used a minimum of analgesics.

TABLE IV

Incidence of forceps delivery 1939	12.84%	(of 4,552)
Incidence of forceps delivery with caudal anesthesia	70.5%	(of 200)
Primigravidas	83.6%	
Multiparas	42.5%	
There were 3 breech deliveries		

Disadvantages

We wish to remind you of an earlier statement that, when continuous caudal anesthesia is successfully established, the patient goes through labor without any discomfort whatsoever. Nevertheless, there are some unpleasant and occasionally dangerous factors in the use of this method which require consideration.

Care must be taken to prevent liquid skin antiseptic running down onto the vulva, where it will burn severely. The knee-chest position is uncomfortable to maintain for long, especially during contractions. The lateral, or modified Sims' position, is satisfactory for the experienced operator, and for patients with excellent landmarks. It should be employed in cardiac patients, and in those having such frequent and hard pains as to make them uncooperative in any other position.

The insertion of the caudal needle is frequently rather painful, though this is reduced by the skillful operator by careful infiltration of

the skin, subcutaneous tissue, and deeper layers adjacent to the periosteum and sacrococcygeal membrane using the same pontocaine solution made up for the caudal. The use of a smaller gauge two inch "finder" needle, through which 4 or 5 c.c. of solution are injected into the tip of the caudal canal when it first penetrates the membrane, decreases the discomfort of the larger following needle. More care to insure an adequate local tissue anesthesia is necessary when the large (15 gauge) catheter-introducing needle is to be employed, as it takes considerable force to introduce it into the caudal canal.

In this series most of the anesthetics were initiated by Dr. Brown, the Director of Anesthesia, or by one of three residents in obstetrics assigned to him for instruction in caudal techniques. A fair proportion of cases, however, was performed by "postgraduate physicians" who come for supervised practical experience in the method. Due to the exigencies of teaching and the difficulties encountered in the early experience of new personnel, the average time recorded in more than half the cases from the skin wheal to the test-dose was 19.6 minutes. This can be reduced to limits of 3 to 10 minutes by the more experienced operator on uncomplicated subjects. The time required to establish accurate insertion has been as much as 40 minutes in some cases. This period may be one of considerable discomfort to some patients. The opinions of the obstetrician and the anesthetist may differ as to the importance and severity of discomfort associated with insertion of the caudal needle or catheter, but in the last analysis, it is the patient who will tell you whether it was worth it, after the dramatic relief of all labor pain is effected.

Among other disadvantages are the potential major complications of circulatory or respiratory depression due to massive intraspinal injection, intravascular injection, unusually high extension in the peridural space, or systemic toxicity due to absorption. By good fortune and rigid adherence to the strict regime of precautions outlined, no such major complication has occurred. It is possible that the selection of pontocaine and the use of a vasoconstrictor (suprarenin) have influenced this favorable experience.

Another practical disadvantage is the time and attention of the administrator required for successful conduct of the method. Although many details of management can be entrusted to a nurse especially trained to this task, the patient must be followed more closely by rectal examinations by the intern or resident, and the anesthetist responsible for the case or one equally competent in judgment and technical facility must be available within the building or on 10-minute call. Frequent problems arise in the management of a caudal case that require experienced appraisal, judgment, and decision, to insure uninterrupted maintenance of relief. It has been the experience of all in our acquaintance who have given a considerable number of continu-

ous caudal anesthesias that as soon as they get far away from the patient something "goes wrong." One must stay within fairly close reach of the nurse supervising the cases to insure their complete success.

Results

One hundred seventy-one cases (85½ per cent) were classified as completely satisfactory. There were only 3 definite failures due to inability to locate the caudal canal. In 10 patients there was initially complete relief, but later the needle became dislodged (5 cases) and was not or could not (1 case) be reinserted, or the needle was removed too soon, or the tubing became disconnected, or the catheter became plugged, resulting in return of pain, all 10 being classified as "technical interruptions" of the method. Six patients had incomplete relief in two of whom anesthesia was unilateral only. In 9 other cases of incomplete anesthesia, the deficiency *was* remedied by technical corrections such as addition of the vasoconstrictor suprerenin (2 cases) where it had been omitted, increase in the concentration of pontocaine (4 cases), and reinsertion of the needle (5 cases). In 1 case the subarachnoid space was entered; in another this was suspected. No complications resulted, but immediate complete relief of labor pain occurred following injection of less than the usual test-dose. Surgical removal of broken caudal needles was necessary in two cases, the break in each case being near the "neck" of the "hubless" Hingson needle. Neither needle possessed the new "safety-bead" designed to prevent disappearance of the needle shaft under the skin. Mild blood pressure fall was recorded in 34 cases, but in only six of these was the fall greater than 30 points systolic. The greatest drop occurred in a mild toxemia in which the pressure fell from 150/100 to 70/40 but it was restored to a safe level by an intravenous infusion of saline and 1 mg. of neosynephrin. Five patients complained of pounding headache during the injection. One complained of momentary chest pain, one of palpitation, and one had nausea and emesis after the first injection. Four had chilly sensations. In three patients severe chills were present after injection, one lasting fifty minutes. Three others developed chills with fever. In one the temperature went to 104° F., and she was disoriented for three hours. In two patients relaxation was so marked that the cervix protruded externally after delivery. Two patients had severe post-partum hemorrhage. There were 13 cases of mild endometritis, 3 of pyelitis and five that required catheterization post partum, which is no more than in cases without caudal anesthesia. Motor loss was present to some degree in 154 cases and in 60 of these it was marked. In most cases the onset of motor paresis was delayed for some time after the first injection. One patient had fecal incontinence for three days. One patient developed anal sphincter relaxation bladder paralysis, and a bilateral foot drop. This patient was a luetic who had received four neosalvarsan injections (2 neo of 0.3 with 0.13 bismuth and 2 neo of 0.6 with 0.13 bismuth) during pregnancy and from whose hair arsenic was recovered post partum. Nevertheless, the paralysis developed during labor. The rectal sphincter gradually regained its tone over a period of ten days but the foot drop improved very slowly and even after nine weeks muscular control is still imperfect.

In our experience labor was not shortened. In six cases labor lasted more than 24 hours after the caudal injections were begun and one of these was a multipara. We were unable to note any evidence of cervical

relaxation due to the anesthetic although there was prompt and complete relaxation of the perineal muscles.

Summary

1. Two hundred cases of continuous caudal anesthesia are presented and discussed mainly from the viewpoint of the obstetrician.

2. Pontocaine-suprarenin-saline solution has proved a safe agent for this method providing 3 to 5 hours of relief from the first dose, and 1 or more hours of relief from subsequent injections.

3. Certain precautions are outlined, but the detailed technique is reserved for another publication. Adherence to a strict regime is advised.

4. Tables are given quoting figures on duration of labor under caudal anesthesia and time required to complete cervical dilatation. We find that cervical dilatation is not accelerated in this series.

5. The incidence of operative deliveries is increased.

6. Several disadvantages of caudal anesthesia are discussed.

7. The results and complications are classified, including 1½ per cent total failures, and 13 per cent additional not completely satisfactory. One hundred seventy-one of 200 cases were completely satisfactory. One prolonged neurological complication is reported.

8. There was no maternal mortality. Fetal mortality was 3.0 per cent.*

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*See Discussion on Symposium on Obstetrical Anesthesia, page 85.

CONTINUOUS CAUDAL ANESTHESIA WITH PROCAINE HYDROCHLORIDE IN 240 OBSTETRIC PATIENTS*

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THE use of continuous caudal anesthesia at the University of Iowa began in August, 1942, and this report is concerned with the first 240 obstetric patients on whom the method was tried. The patients were largely unselected, although the major obstetric complications were avoided. Nine men were responsible for the administration of the anesthetic, a fact which must be borne in mind when the failures in this series are discussed, since it is well recognized that technical proficiency in introducing a needle into the caudal canal is important.

Method

The catheter technique was employed universally. A number 13 gauge, 3½ inch needle was inserted into the caudal canal and a number 5 ureteral catheter threaded through it. Procaine hydrochloride, generally 1.5 per cent in saline solution, was the anesthetic agent, although a 2 per cent solution was used occasionally. The standard dose was 30 cubic centimeters, although varied sometimes to suit individual reaction. As a prophylactic against any possible toxic effects of the drug, 1.5 grains of sodium pentobarbital (nembutal) were given orally prior to introduction of procaine. Believing that the rates of absorption and excretion were more important than the amount administered at any one given time, doses were recorded as milligrams per hour and ranged from 400 to 600. As a working rule, no anesthetic was continued more than 24 hours.

Results

Excellent results (total elimination of pain) were obtained in 68 per cent of the patients. Fair results were obtained in 12.0 per cent, poor in 2.5 per cent, while failure occurred in 16.9 per cent (39 patients). The operator failed to introduce the needle into the caudal canal in 18 instances: In two cases spinal fluid was encountered and the procedure immediately abandoned. In 11 patients the anesthetic was discontinued, 3 times accidentally and 8 deliberately because the patient either was not in labor or was experiencing a prolonged labor. In 8 instances, the cause of failure was not specified. In general, it may be said that anesthesia will always be satisfactory if: (1) the apparatus is placed, and remains, in the caudal canal; (2) if sufficient anesthetic is introduced.

*Read at a meeting of the Chicago Gynecological Society, October 15, 1943.

Effect on Labor

The figures have not been analyzed with regard to the total length of labor, since the series is entirely too small to warrant conclusions in this regard. It is, however, the clinical impression of those who participated in the study that the first stage of labor is somewhat accelerated while the second is markedly retarded. For example 35.4 per cent of the patients in the present series (primigravidas 63.7, multigravidas 10.2) required forceps operation. These figures are considerably in excess of the usually conservative clinic incidence of employment of forceps at the University Hospitals, although indications were not altered. Moreover, the definite clinical impression was obtained that spontaneous rotation from an occiput posterior or transverse position was interfered with, since the incidence of manual or forceps rotations was definitely increased.

Significant blood pressure depressions were noted in a certain number of patients, although this fact was not appreciated at first. In the last 136 patients, depression of systolic pressure below 80 millimeters (Hg) was noted in 13 or 9.6 per cent. This fall was readily combated by the *simultaneous* administration of ¾ grain ephedrine sulfate, ⅜ grain intravenously and ⅜ grain intramuscularly. Such blood pressure drops are now anticipated through careful observation and ephedrine administered prophylactically, when indicated.

Effect on the Mother

There were no maternal deaths and no postanesthetic paralyses of legs, anal or bladder sphincters by the time (average 10 days) the patient left the hospital. The maternal complications included: Two superficial infections which healed without surgical intervention and which did not cause any neurologic symptoms; 2 subarachnoid punctures followed by immediate abandonment of the procedure; 1 generalized muscle twitching subsiding spontaneously without recurrence despite subsequent reinjections of procaine; 2 patients transiently developing unilateral Horner's syndrome, i.e. mydriasis, widening of the palpebral fissure and slight exophthalmus; 1 catheter cut off. This last accident occurred because the operator, believing the introducing needle was not in the caudal space, withdrew the catheter without first withdrawing the needle. Two centimeters of the catheter were cut off and remained in the caudal canal. No serious operative attempt was made to remove the end of the catheter and the patient suffered no consequences.

Effect on the Infant

There were 2 fetal deaths in a series of 201 patients (240 less 39 failures) but neither death was attributable to the anesthetic. There was one other fetal death but this occurred in one of the 39 cases of failure where no procaine was injected. One hundred seventy-three

(86 per cent) of the children cried spontaneously immediately after birth and in some instances before the shoulders were extracted. Nineteen (9.5 per cent) exhibited a very slight delay in breathing, but in no case more than 2 minutes. Only 3.5 per cent required any resuscitative measures because of asphyxia.

Indications and Contraindications

Continuous caudal anesthesia was administered to certain patients with heart disease, one of whom was a grade III. Her labor was so smooth and the effect on the heart so negligible, it might seem as if this is a very desirable method of anesthetizing cardiac patients.

Because there is practically no effect on the infant, it would also seem that the continuous caudal technique might solve the problem of asphyxia in relation to analgesia and anesthesia for women in premature labor.

The method is contraindicated whenever a test of labor is necessary, since no test can be adequate without the full, voluntary cooperation of the parturient.

Comment

It is premature to predict the future place of continuous caudal anesthesia. The method is time-consuming and there can be no doubt that it possesses potential dangers. These risks may be largely minimized and often eliminated when the method is employed with intelligence and meticulous attention to detail. However, this objection alone should be sufficient to preclude its routine use. The physician employing continuous caudal anesthesia must personally supervise every detail. There should be no delegation of any part of the technical performance to others. On the other hand, it is a remarkable method which comes close to satisfying the requirements of an ideal obstetric anesthetic agent. In selected patients, provided the physician is adequately trained and is prepared to be in constant attendance throughout the course of the anesthetic, it would seem to be a satisfactory method.*

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*See Discussion on Symposium on Obstetrical Anesthesia, page 85.

CONTINUOUS CAUDAL ANALGESIA IN OBSTETRICS

A Commentary

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AT THE Baltimore City Hospitals, in 1938, caudal anesthesia in obstetrics was subjected to a critical study by a group of resident obstetricians, under my supervision. We confirmed previous investigators' observations, viz.; a single injection of anesthetic agent through the sacral hiatus would produce complete relief from pain for the parturient in active labor regardless of the stage of labor and this analgesia would be accompanied by classical caudal anesthesia and marked perineal relaxation. Such obtundity phenomena persisted for approximately one hour after which time they gradually disappeared. The uterine contractions continued without interruption throughout the period of anesthesia. We also found that if we reinserted the needle in the caudal canal and injected a repeat does of anesthetic agent when the effect of the previous injection was beginning to disappear, satisfactory anesthesia would continue on for another hour. In other words, we could produce continuous analgesia and anesthesia by a continual administration of anesthetic solution by single injections at appropriate intervals. We studied a small series of cases in which this continuous anesthesia was maintained by repeated injections, beginning at various stages of labor. We hoped to find that labor would progress normally to a spontaneous delivery without pain but we were disappointed. Although we found that cervical dilatation would frequently progress satisfactorily if the presenting part were deeply engaged, if the presenting part were in high pelvis the first stage was sometimes considerably retarded. To our further disappointment we found that in the large majority of cases the second stage was retarded and in almost all cases was arrested. Although some descent usually occurred the presenting part was usually arrested in low pelvis and we were forced to follow one of two courses: delivery by forceps from the arrested station or, allow the patient to recover from the anesthesia and complete the labor by the usual painful second stage. When we followed the latter course we found ourselves dealing with an unmanageable patient who demanded another injection of that "wonderful medicine." This reaction is quite understandable to anyone who has witnessed the dramatic relief of pain with caudal anesthesia. When we delivered these "arrested" heads by forceps we realized that we were rarely performing an "outlet forceps" and too often not a very "low" forceps.

Delivery of all primigravidas by outlet forceps and episiotomy was the established routine of the clinic at the time of our study of caudal anesthesia. I think we were completely aware of what an outlet forceps delivery really means and herein lies a very important issue. When the head has traveled beneath the pubic arch and begins to crown and is then delivered by forceps, such a delivery is correctly an outlet forceps. In this type of delivery the forceps are used for extension but not traction. A head delivered from any higher station ceases to be an outlet forceps and is accomplished principally by traction to bring the head beneath the pubic arch.

Most trained obstetricians feel that elective episiotomy and outlet forceps delivery are justifiable because of both immediate and remote advantages, but these obstetricians also know that elective delivery of a head from a higher station is unjustifiable and constitutes poor obstetric judgment. It is true that a trained operator may deliver from a higher station with a satisfactory outcome when the procedure is indicated and necessary, but he does not elect to do it because he knows that such deliveries are frequently the antecedents of pathologic relaxation of pelvic supporting tissues.

Our experience with caudal anesthesia, therefore, indicated that if the anesthetic were administered somewhere in the middle of labor, we were forced to terminate the labor by what our guided experience dictated was "bad obstetrics." It is true that occasionally a multipara could be encouraged to terminate the labor spontaneously by requesting the patient to bear down when she had a painless contraction, but these cases were the conspicuous exceptions. In most primigravidas with such encouragement the head would not descend to a station from which the delivery could conscientiously be labeled an outlet forceps.

Our conclusions from this study of caudal anesthesia indicated that its use to eliminate first- and second-stage pain was inadvisable because of the interference with the normal mechanism of labor. We concluded that it does have many desirable advantages as an anesthetic for delivery in selected cases when operative delivery is indicated. For such purposes a single injection usually affords sufficient anesthesia time. We also pointed out that the administration of a caudal anesthetic, no matter when administered, is potentially dangerous. And although, by exercising intelligent caution, this danger may be minimized it cannot be entirely eliminated. It seemed to us, therefore, that a caudal anesthesia used as an analgesia is inadvisable. Even as a routine delivery anesthetic it is unjustifiable and should be used only in selected cases. If our factual findings are accurate I believe anyone interested in a higher order of obstetrics will agree with the conclusions. A detailed report of our study and conclusions were duly recorded.[1]

We overconfidently ignored our own published counsel and following the completion of our series for publication, the procedure was con-

tinued as a routine delivery anesthetic on the obstetric service. The administration of the anesthetic to approximately our six hundredth case resulted in an accidental intradural injection with sudden respiratory failure. The administration of intratracheal oxygen, artificial respiration and lumbar puncture and withdrawal of spinal fluid (contained anesthetic) resulted in the resumption of spontaneous respiration after twenty anxious minutes. This particular anesthetic was administered by an experienced operater who had taken the usual precautions to exclude intradural and intravenous injection. Our confidence was shaken and caudal anesthesia was discontinued as a routine anesthetic. Our enthusiasm for the procedure was being shared by two other large maternity clinics in Baltimore (The Johns Hopkins Hospital and University of Maryland Hospital) where it was being used cautiously. At the Johns Hopkins Hospital in March, 1940, caudal anesthesia was administered to the one hundredth obstetric patient and two minutes later the patient was dead. All customary safety precautions had been observed. Post-mortem study revealed the presence of the anesthetic solution in the spinal fluid. The procedure was thereafter abandoned at the Johns Hopkins Hospital. The procedure was continued at the University of Maryland Hospital until August, 1940, when a caudal anesthetic was administered and the patient observed for five minutes. The attendant left the patient and returned a few minutes later to find the patient dead. In this case the post-mortem spinal fluid contained no evidence of anesthetic solution. Thus the season of caudal anesthesia was terminated at another hospital when the procedure was abandoned at the University Hospital.

Investigation subsequent to our original report indicates that our conclusions regarding the incidence of comparatively high pelvic arrest represented a sampling error. Hopp[2] was the first to point out that many labors were not arrested under fractional doses of caudal anesthesia. In 1941, Hopp[2] published the first report on a series of cases in which he used continuous caudal anesthesia to produce painless labor and delivery. His series was small and apparently attracted little attention. Hopp's principle was highly publicized by Hingson and Edwards in September, 1942,[3] and continued with increasing fervor through 1943,[4-9] with Hopp's contribution conspicuously ignored. Such persistent zeal is unprecedented in the long line of previous caudal anesthesia enthusiasts. A panoramic view reveals the history of twentieth century obstetrics punctuated with waves of enthusiasm for caudal anesthesia. The present wave of enthusiasm, however, is of such magnitude that it is unquestionably the outstanding topic in American obstetrics today. The reason, I think, is not because of any significant scientific advancement in the application of the principle of caudal anesthesia in obstetrics but the answer lies in the power of the public press. Medical science has not discovered anything new but the lay press has. Expectant mothers all over the country are requesting what

has been misrepresented to them as "safe, painless childbirth." The movement has to some extent stunned the medical profession to the point of clouding its judgment. Even without this influence the average physician is moved beyond reason when he first witnesses the dramatic relief of pain the parturient experiences under caudal anesthesia. Unfortunately, most physicians were caught in this surge of enthusiasm originating in the lay press before they knew what caudal anesthesia in obstetrics was all about and they could not combat it. Their impulse was to jump on the band wagon and ride along. Such reactions, of course, will be only temporary and there are signs on the horizon now indicating that the skies are beginning to clear. Physicians are beginning to awaken to actual facts. Witness the increasing accuracy of interpretation of their own factual findings in the publications of Hingson and Edwards, the chief sponsors of the movement. In their first reported cases they thought they were doing elective forceps deliveries[3] and implied that the anesthesia was not interfering with the normal course of labor. However, in their most recent report[9] they are apparently willing to recognize this interference. They admit, "The incidence of operative obstetrics is increased. No physician should use continuous caudal analgesia unless he is well trained in the use of forceps. The incidence of posterior positions and transverse arrests in midpelvis is increased." And finally, the incriminating admission that "the entire course of labor is altered from the picture described in textbooks."

It is incredible that the leaders of American obstetrics will allow such admissions to go unchallenged. The science and art of obstetrics are built on the concept of the normal mechanism of labor. In our search for the ideal obstetrical analgesia we have always insisted on the rigid adherence to the criterion of "no increase in operative deliveries." Hingson and Edwards would rely on the perineal relaxation to justify their obligatory forceps deliveries. It is true that the muscular relaxation does facilitate the immediate problem of delivery to a degree but caudal anesthesia does not relax the bony pelvic ring. The sequelae of forceps deliveries do not usually become manifest until some time later. Every gynecologist realizes that many of his plastic operations are necessitated because of a forceps delivery done some years before. Hingson and Edwards recommend delivering the patient "when the presenting part can be seen by spreading the vulva."[6] In this role the relaxed perineum becomes a two-edged sword in that one can visualize the presenting part at a comparatively high station when the relaxed perineal muscles are spread apart. As I witnessed the motion picture on caudal anesthesia which is being shown and watched the depiction of the terminal stages of an axis-traction forceps delivery, I wondered where in the pelvis this head might have been when the delivery was started. That part of the delivery is not shown. I also wondered if that patient will be consulting a gynecologist ten years hence.

Caudal anesthesia is no safer today than it ever was. The present practice of using an indwelling needle or catheter in the sacral canal between injections has done nothing but increase the hazards. Although the ever present danger of vascular collapse probably remains the same, the risk of accidental dural penetration is increased. The hazards of needle breakage and infection have been added. The fact that any therapeutic procedure carries a risk does not necessarily condemn its use in medical practice, the art and science of which is made up largely of the balancing of risks and probabilities. However, the use of such a hazardous procedure *electively* to relieve the usually innocous pains of labor is unjustifiable. Since the recent advent of continuous caudal analgesia four women have lost their lives because of the procedure per se.[8, 10-12] There have been other "close calls" reported. There must be other fatal or near fatal accidents which were not reported. Never before has the human nervous system been subjected to the action of such prolonged concentrated anesthesia. The absence of residuals and sequelae remains to be proved. Suggestive evidence of some neurologic damage has already come forth[13] and this lead is being followed through by experimental animal investigation, as it should be.

When one contemplates the future of continuous caudal analgesia, it would seem important to realize that for many years disciples of caudal anesthesia have frequently appeared on the medical horizon. They have fanatically recommended its use in urology, proctology, gynecology and obstetrics but practically all of these enthusiasts have eventually abandoned the procedure. Some surrendered soon because of the technical difficulty of administration but others who mastered the technique gave up later because of the inherent hazards in the principle. It seems strange that the tragic accidents are so frequently delayed in any one man's experience, but apparently they eventually do occur. I predict they will come to those who are now promoting continuous caudal analgesia. However, even if we assume they will not occur there are other disadvantages to the procedure which preclude its very general application. The procedure is laboriously time consuming. Busy obstetricians, anesthetists, or house officers would have time for nothing else. The financial obligation involved for expert supervision and administration would be prohibitive for most patients.

The fact that the promoters of this movement are conducting a "school" in which a general practitioner, untrained in obstetrics, may administer a few caudal anesthetics to women in labor and then "observe" the delivery of these patients would seem open to serious criticism. Such a practice is a reckless method of evaluating the procedure. The incidence of complications will be inversely proportional to the obstetric judgment and dexterity of those who use it.

The test of time will put continuous caudal analgesia in its appropriate place in obstetrics and until this comes about we must hope that the

minimum number of mothers will suffer harm. Contemplation of the appropriate place of this procedure reminds one of the episode of the elective version of Potter and his disciples who threatened to revolutionize obstetrics by a procedure which interfered with the normal mechanism of labor in order to bring relief to women in labor. The test of time settled the Potter version, appropriately, in the footnotes of the history of American obstetrics. Despite the initial fanfare, I suspect much the same fate for continuous caudal analgesia. Although its occasional use in accurately selected cases may give it some degree of permanence, I predict it will never become generally used in obstetric practice.

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CYCLOPROPANE-PITUITRIN INCOMPATIBILITY

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IT IS surprising to note the paucity of cases of pituitrin shock, especially of those with fatal result, reported in the literature. It is probable that the condition is not as rare as this would indicate, but its occurrence should be kept in mind. The lack of reports is probably due to the failure of the anesthetist or obstetrician to recognize the picture when it presented itself, the diagnosis of pulmonary embolus, shock, coronary occlusion, or anesthetic death being made without considering the possibility of drug susceptibility. These mistaken diagnoses are readily understood since this is often the picture exhibited, but the underlying cause has not been appreciated.

In this paper we should like to point out the basic pharmacologic facts with reports of two cases witnessed.

Pharmacology

Cyclopropane is a very potent hydrocarbon capable of producing surgical anesthesia in concentrations permitting a high percentage of oxygen in the mixture. For this reason, it has come to be demanded by obstetricians when doing cesarean sections, and rightly so, because of the short induction period and the benefits of high oxygenation to mother and child.

Pharmacologically, cyclopropane is a stimulant of the parasympathetic system. It causes bronchoconstriction, which may induce an asthmatic attack in a susceptible patient. It also has a tendency to produce all sorts of cardiac arrhythmias with displacements of the rhythm centers, ranging from bradycardia to ventricular fibrillation.

Pituitrin, an extract of the posterior pituitary gland, has four principal actions. It stimulates the myometrium, causing contraction of the uterus, constricts the capillaries and smaller arterioles by direct action on the muscle cells; stimulates the intestinal musculature to contraction by direct action on the muscle layers; and has a pronounced antidiuretic action by causing maximum reabsorption by the cells in the loops of Henle. The actions primarily affecting our problem are the contraction of the uterus, and the undesirable side effect of constriction of the coronary vessels.[5] Burstein[3] has also pointed out that it intensified the bronchoconstrictive action of cyclopropane, which he found when investigating pitressin, the pressor fraction of pituitrin.

Pituitrin may produce reactions of three types: anaphylactic, cardiac, or respiratory. The first is not particularly dangerous, especially when not in conjunction with cyclopropane anesthesia, and the recovery from the shocklike symptoms with urticaria, itching, and angioneurotic

edema is rapid upon the administration of a few minims of adrenalin. Pituitrin shock due to the action of the pressor fraction on the heart is attributed to coronary constriction followed by myocardial anoxia, dilatation of the heart, decrease in cardiac output, and fall in blood pressure, with sometimes a fatal outcome. The respiratory reactions are signified by bronchoconstriction of varying degree, simulating an asthmatic attack.

Pituitrin is marketed in two forms, which vary only in strength, obstetrical pituitrin having 10 units per c.c., and the surgical form 20 units per c.c. It has been broken up into its fractions, and is obtainable as "pitocin," containing the oxytocic fraction with a very small amount of the pressor fraction, and "pitressin," which is almost purely the pressor fraction with only slight contamination by the oxytocic fraction. Pitocin, rather than pituitrin, is then evidently the drug of choice in obstetrics.

The combined use of cyclopropane and pituitrin is fraught with danger since they are both parasympathetic stimulants. In the circulatory system they have a synergistic tendency toward the production of hypertension and/or cardiac arrhythmias. From the parasympathetic stimulation of the respiratory tract they may produce laryngospasm, crowing, stridor, or bronchoconstriction, which may range from asthmatic wheezing to massive collapse of the lungs. The bradycardia often seen may be due to vagal stimulation, direct myocardial action, or intense coronary constriction.

Case Reports

CASE 1.—Mrs. S. G., a 30-year-old primipara, was admitted to the Adelphi Hospital, Brooklyn, N. Y., on December 6, 1942, with ruptured membranes and irregular pains. She was obese, of a type suggesting an endocrine imbalance, with an ample pelvis. The blood pressure was 120/80, and the physical findings essentially negative except for obesity.

She was in labor until December 10, 1942, with irregular pains of moderate severity, but requiring morphine plus scopolamine sedation because of her uncooperative nature and meager intelligence. The cervical dilatation progressed slowly over this period to 3 cm. At this time a consent for cesarean section was finally obtained.

At 9:25 P.M. on December 10, 1942, anesthesia with a mixture of cyclopropane and oxygen was started, the patient having had no preanesthetic medication. A Waters' cesarean section was started at 9:37 P.M., and a normal living child delivered at 10:40 P.M. Ergotrate and pituitrin were then given to contract the uterus and control the bleeding. The pulse, which had been about 110, now rose to 130 and remained between 130 and 140, full and bounding, for the remainder of the operation, which ended at 11:30 P.M. At the close of the operation, when the mask was removed from the patient's face, she became cyanotic, and oxygen was administered, with a rapid improvement in the patient's color. She was watched for about fifteen minutes and then removed to her room. Upon arrival there at 12:00 midnight she was

reacting, became very restless, requiring several attendants to restrain her. Her heart rate had risen to 200, she rapidly became cyanotic, and succumbed at 12:50 A.M., in spite of strenuous supportive measures. Permission for autopsy was not obtained.

On the basis of the clinical findings, we feel that this patient had a massive atelectasis, which probably was precipitated by the combined bronchoconstrictor actions of pituitrin and cyclopropane. The possibility of cyclopropane alone producing this atelectasis is strong, but it was undoubtedly greatly aggravated by the pituitrin.

CASE 2.—Mrs. C. K., a 35-year-old primipara, was admitted to the Lenox Hill Hospital at 6:30 A.M. on November 10, 1943, thirty-five weeks pregnant, with a history of having had severe cramps associated with moderate bleeding the preceding evening. At 8:30 the fetal heart had become irregular and rapid, and a cesarean section was decided upon. Preanesthetic medication of atropine gr. $\frac{1}{150}$ was given at 8:45 A.M.

Induction of anesthesia, using a cyclopropane-oxygen mixture, was started at 9:17, and after an infusion was begun, the operation commenced at 9:29. Up to the time of delivery of a normal living child at 9:40, the pulse had remained fairly constant between 96 and 116, and the blood pressure at about 130/80.

At 9:41, pituitrin, 1 c.c. was injected into the uterus and ergotrate, 1 c.c. given intravenously. At 9:45 the pulse was 132, and then at 9:48 had dropped to 76. At 9:50 the pulse was 176, and morphine sulfate, gr. $\frac{1}{8}$ was given intravenously. At 10:00 the respirations had become somewhat depressed, but responded to coramine and metrazol, 1 c.c. each. At 9:45 small amounts of ether were added to the anesthetic mixture, and the cyclopropane discontinued. At 10:05, 500 c.c. of blood were added to the infusion. From now until the end of the operation at 10:25, the pulse varied markedly between 76 and 164, weak, fairly regular, at times unobtainable.

At 10:40 the patient had fully reacted and was extremely restless, with a feeble rapid pulse, pale, and throwing her arms around, dislodging the infusion. Oxygen was administered intermittently after the close of the operation. Pantopon, gr. $\frac{1}{3}$ was given at 10:50, at which time the patient was pale, with a trace of cyanosis, and oxygen was being administered continuously. At this time, the condition of the patient appeared very grave, and intravenous therapy of blood (500 c.c.) and plasma (500 c.c.) was started in both arms, between 11:00 and 11:15. Her respirations were shallow. Neosynephrin, coramine, metrazol, and adrenal cortex were given intravenously from 11:15 to 11:30 with no result. Her pulse and blood pressure were not obtainable now, and very shallow respirations were being reinforced by positive pressure on the rebreathing bag. At 12:15 the heart beats could no longer be heard, the respirations were maintained with the anesthesia machine and then with an E & J Resuscitator, while intensive stimulation was again given until 12:55, when the patient was pronounced dead.

At autopsy, the only positive findings were some small atelectatic areas in the lungs with no signs of a pulmonary or coronary embolus. There had been no postoperative intra-abdominal bleeding.

In this case, the injection of pituitrin precipitated a severe cardiac derangement. The pulse became uncontrollable, with marked variations, followed by a progressive circulatory collapse. During the close of the operation, the combined effects of ether with a high oxygen con-

centration and stimulants helped maintain the patient's condition, but when the anesthesia was discontinued, she rapidly declined and could not be revived. The ether was given too late in an attempt to stabilize the patient. Undoubtedly, this was a severe form of the cardiovascular type of pituitrin shock due to the combined actions of pituitrin causing myocardial anoxia and cyclopropane disturbing the rhythm centers. The small atelectatic areas in the lungs, found at post mortem, were not enough to have caused this picture.

Discussion

Pituitrin shock has been reported several times in the literature. Bickers[2] reported an interesting case of an anaphylactic reaction in a multiparous woman at two successive deliveries after the administration of pituitrin, only the second of which was diagnosed and cured immediately with adrenalin. Greene[4] has reported unfavorable reactions from the use of pituitrin in surgical procedures being done under cyclopropane anesthesia. In a series of seven cases of pituitrin shock in patients undergoing surgical procedures, such as hysterectomy by the vaginal route, where pituitrin was injected into the uterus to minimize bleeding, observed by Adelman and Lennon,[1] there were no fatalities.

In one of our cases, the depression of respiration and bronchoconstrictive effects of cyclopropane combined with the bronchoconstriction of the pituitrin produced a massive collapse of the lungs which was not disclosed while the patient was receiving a high concentration of oxygen. In the other case, the synergistic actions of the cyclopropane and pituitrin served to produce a condition of shock leading to anoxia which was irreversible. It was partially disguised during the anesthesia but once this was discontinued, the status of the patient rapidly became worse, and in spite of strong resuscitative measures, there was a fatality.

Although pituitrin has been used in connection with cyclopropane in many cases where no untoward reactions were noted, this does not absolve the combination of blame. It is in those cases where the patient probably would have had a reaction from pituitrin under any anesthetic that the severe pictures here presented have occurred. Greene[4] has recommended adding ether to the anesthetic mixture if pituitrin is to be used, depending upon the sympathetic action of the ether to counteract the parasympathetic effects of the pituitrin and cyclopropane.

Comment

Pituitrin shock is greatly accentuated when it occurs under cyclopropane anesthesia, and may cause a fatality. There are two ways to prevent this: first, by using ether along with the cyclopropane; and secondly, by not using pituitrin. Pitocin, the oxytocic fraction of pituitrin, is just as good in causing uterine contraction, without any of

the side effects of pituitrin, and in many obstetric clinics has supplanted it. Ergonovine in any of its forms is an excellent and rapidly acting oxytocic and can be used for this purpose instead of pituitrin. by using either of these alternatives, an extremely unfortunate accident can be avoided.

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INTERSTITIAL ECTOPIC PREGNANCY

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CARL H. DAVIS states that according to modern statistics, ectopic pregnancies vary in incidence from 3.3 cases in 1,000 pregnancies (these being the figures in Schumann's series) to 13 cases in 1,000 pregnancies (Wynn in the Johns Hopkins series).[1] The same author states that pregnancy in the intrauterine portion of the Fallopian tube, so-called interstitial pregnancy, occurs in less than 5 per cent of all ectopic pregnancies.[2] On the basis of these figures, interstitial pregnancy should occur less than once in 6,000 pregnancies to a maximum of less than once in 2,000 pregnancies. Accordingly, we may consider interstitial pregnancy a relatively uncommon occurrence.[3] Because of that fact and in order to show the similarity and dissimilarity in the clinical picture, gravity and termination that may exist in two cases of interstitial pregnancy of about the same period of gestation, the author feels justified in presenting the following two cases.

CASE 1.—Mrs. L. H., colored, 18 years of age, was admitted by ambulance to the medical service of the hospital with the diagnosis of acute food poisoning. Soon after admission, she was transferred to the surgical division, June 16, 1942.

Her family history and past medical history were noncontributory. In December, 1941, she had had a premature eight months' infant.

Present Illness.—Her last period occurred approximately March 28, 1942. On May 8, 1942, while standing, she aborted a six weeks' fetus (unconfirmed statement of the patient). This was followed by bleeding. The bleeding stopped during the night of May 8, but started again on May 9, and she went to a hospital where she remained until May 15, at which time she was discharged with a diagnosis of spontaneous complete early abortion and hypochromic anemia. After returning home, she still felt weak and morning nausea and vomiting continued. On June 16, 1942, at about 1:45 P.M. she developed sudden acute pain beginning in the right lower abdominal quadrant; she felt weak and is said to have fainted. She attributed her sudden distress to some food.

Examination on Admission.—Patient acutely ill, in severe pain with marked pallor and cold extremities; temperature 98.6° F., pulse 84, respirations 20, blood pressure 84/60. Breasts showed colostrum. Abdomen rigid, extremely tender with rebound tenderness, and the maximum point of tenderness is in the right lower quadrant where a mass the size of a walnut can be felt above the pubic crest. Pelvic examination revealed a soft cervix low in the vagina and tender on motion. The fundus uteri was slightly enlarged and displaced slightly to the left of the midline, apparently by the mass on the right.

The laboratory findings were as follows: Urine, negative, blood, hemoglobin 50 per cent, erythrocytes 3,850,000, leucocytes 9,200 with 80 per cent polymorphonuclears and 20 per cent lymphocytes. The Wassermann was negative. Blood immediately typed and voluntary donors sought.

The diagnosis was ruptured ectopic pregnancy, probably in the right tube with the tube plastered against the anterior abdominal wall.

I saw the case shortly after, and immediate operation was ordered.

Operation was done 2 hours and 15 minutes after admission to the hospital, and a little over an hour after transfer to the surgical division. Under cyclopropane and oxygen anesthesia, a right paramedian incision from umbilicus to symphysis was made. Upon opening the peritoneal cavity, there was a tremendous gush of fluid blood under pressure. The mass on the right was drawn out of the abdomen and clamped at its base with two Keith clamps, one on each side (Fig. 1).

Fig. 1.—Case 1. Ruptured interstitial pregnancy at 11 weeks. Most of the free blood and blood clots, with the exception of the blood clots in the cul-de-sac and deep pelvis, have been removed. Ruptured right cornua with chorion extruded and clamps in place are shown. Note that the extrauterine portions of both tubes are uninvolved. A fetus of about 11 weeks lies among blood clots in the cul-de-sac.

This produced immediate and absolute hemastasis. There was at least a liter or more of free blood and clots in the peritoneal cavity. The mass at the right cornua was about the size of a small orange, it arose mesial to the beginning of the right Fallopian tube proper and the right round ligament, both of these structures being entirely independent of the cornual mass and entirely normal throughout. The uterus was only slightly enlarged; the left tube, left round ligament and both ovaries were normal. The mass had ruptured on its dome for about 1½ inches, chorion extruded from the rent and a ten to eleven weeks' fetus lay unattached on the remaining blood clots in the cul-de-sac. The condition of the fetus indicated that it was in all probability alive until the time of rupture.

The mass was cut off above the clamps; several overlapping mattress sutures were placed beneath the clamps controlling the entire base. The serosal edge of the stump was now sutured with a fine chromic suture. The abdomen was closed in layers, using clips in the skin and silkworm-gut tension sutures with Davey buttons. Operative time was 55 minutes.

The postoperative reaction was good, nevertheless, 500 c.c. of citrated blood were given on the night of operation. There was a moderate febrile reaction during the first five postoperative days with a maximum temperature of 102° F. per rectum. The pulse was excellent throughout being 90 or less with one exceptional rise to 100.

Ten days postoperatively examination showed an abdominal wound healed by primary intention with an entirely negative pelvis other than slight tenderness in the right fornix. The patient was discharged June 27, the eleventh postoperative day.

CASE 2.—Mrs. G. N., colored, 28 years of age, walked into the hospital at 9:30 P.M., Oct. 23, 1942, complaining of left lower quadrant abdominal pain. Her family history was noncontributory. Her personal past history: Seven and again four years prior to admission, she had been told that she had inflammation of the tubes and ovaries. Since June, 1941, she has had a creamy irritating vaginal discharge.

Present Illness.—Her last menstrual period of two days' duration occurred approximately July 28 to 30, about twelve weeks before her present admission to the hospital. On September 10, six weeks later, she had a miscarriage but did not seek medical care. She had cramplike pains which started after the "miscarriage"; the pains lasted for several hours and disappeared for two weeks; since then the pain has been intermittent and mild.

Laboratory Findings.—Urine, negative, blood, hemoglobin, 72 per cent, erythrocytes, 3,700,000, leucocytes, 22,500 with 84 per cent polymorphonuclears, 15 per cent lymphocytes, and 1 per cent basophiles. The Wassermann was negative.

I examined this patient shortly after admission and the important pelvic findings were as follows: the cervix showed no definite changes in consistency or color and was not tender on motion or otherwise; the uterine fundus was only slightly enlarged and showed no variation in consistency; the right half could be well defined and was essentially negative; perched on top of the left uterine cornua, there was a definite, round, only slightly tender mass about 2 inches in diameter. The fornices, cul-de-sac and rectum were otherwise negative.

*Operation.**—Under cyclopropane, oxygen and ether anesthesia a left paramedian incision was made from umbilicus to symphysis. The uterus proper was not enlarged and was in good position. Both ovaries and the right tube and round ligament were entirely normal; perched on the left cornua of the uterus and arising from same by a broad base was a round mass the size of a tangerine (Figs. 2 and 3). On one side and over the dome of the mass, the omentum was densely adherent and at the firmest point of attachment, it was darkly stained with old blood pigment (Fig. 2). The omentum was ligated and cut just prox-

*This patient's hospital record failed to show that any vaginal examination had been made; furthermore, there was no gross nor microscopic tissue examination made. A preoperative diagnosis of terminated left interstitial pregnancy was made in this case. This was made possible by the history and course, and particularly by a mental comparison of the physical findings in Case 2 as compared to the operative findings in Case 1, both being of almost identical periods of gestation as to duration and occurring a little over four months apart.

imal to its attachment to the mass, and by lifting the mass upward and forward, it could now be seen that the beginning of the extrauterine portion of the left tube was part of the posterior and inferior aspect of the mass (Fig. 3) and on the lower anterior aspect, the left round ligament formed part of the mass, which could be demonstrated by retroverting the uterus. The tube beyond the point of fusion with the mass

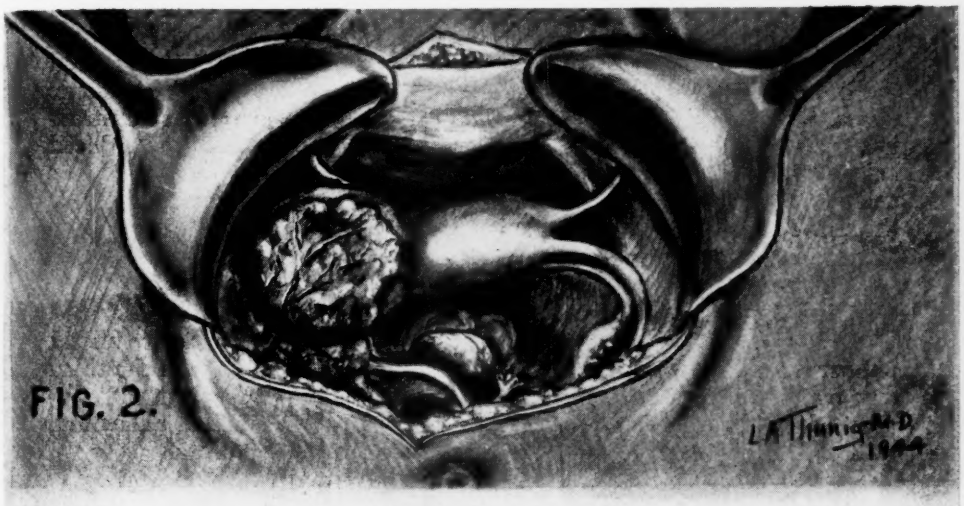

FIG. 3

FIG. 4.

Fig. 2.—Case 2. Round mass at left cornua partly covered by densely adherent and bloodstained (old) omentum.

Fig. 3.—Omentum has been severed and mass lifted. Left tube forming part of cornual mass posteriorly and inferiorly, and left round ligament anteriorly and inferiorly, have both been ligated and cut, the first turn in the knot from a single strand from each ligature denotes method of tying cut ends together. Clamp has been placed across cornua and overlapping mattress sutures placed, the outermost one of which has been purposely drawn slightly heavier, encircles the upper part of uterine artery.

Fig. 4.—Section of left cornua. The stump showing is the tube. Round ligament is also present but not in view. Structures represented from without inward are: adherent omentum, muscular wall of the cornua, blood clot, fibrin and occasional chorionic villus, amnion and 1.3 cm. attached fetus.

was entirely normal; the same held true of the left round ligament. The tube, ovarian artery and a portion of the left broad ligament were doubly ligated about ½ inch from the mass and cut between ligatures; the round ligament was treated in the same fashion. A single curved Keith clamp was placed across the base of the mass just below the level of the stumps of the tube and round ligament (Fig. 3). The distal ends of the round ligament and tube were tied together. The mass was cut off above the level of the clamp. The specimen was sectioned in the operating room and showed a condition as portrayed in Fig. 4. Outer layer consisted of uterine muscle, then came a layer of old organized blood clot with considerable fibrin but only an occasional chorionic villus, then the intact amnion with a 1.3 cm. attached fetus of approximately six weeks. Several overlapping mattress sutures were placed below the clamp, the outermost one being placed to encircle the upper end of the uterine artery (Fig. 3). This formed a groove into which the united ends of tube and round ligament were sutured. The area was then peritonealized by suturing the edges of the lips together over the buried tube and round ligament with a continuous suture.

The patient's postoperative course was uneventful. There was a moderate febrile reaction for the first two days with a maximum rectal temperature of 102.4° F., and a maximum pulse of 120. From the third day on, pulse and temperature were normal and the patient was discharged on the eighth postoperative day with a clean-healed abdominal wall and an entirely negative pelvis and abdomen.

Conclusions

1. Interstitial pregnancies are relatively uncommon.

2. Interstitial pregnancies, even though of about the same period of gestation and similar in some respects, may vary greatly in symptomatology, termination and prognosis.

3. Never accept a patient's statement concerning the occurrence of an abortion unless you personally see the products of conception.

4. These two cases show, as has already been emphasized by so many authors, that every unproved abortion should be suspected of being an ectopic pregnancy until proved otherwise. Observance of this rule would prevent many catastrophies.

5. The presence of a well-defined tumor at the cornua of the uterus with a history suggestive of extrauterine pregnancy should lead one to suspect an interstitial pregnancy.

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1172 Dean Street

SARCOMA BOTRYOIDES

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IN THE rather extensive literature that has grown up on the subject of sarcoma botryoides, McFarland's articles,[11, 12] together with their associated bibliography, are the most comprehensive to date. As a matter of record and owing to the rarity of the condition in children, the following case is presented for its clinical and pathological interest. The disease ran its course in seven months from the date of onset of symptoms until its termination in August. The patient was inoperable when first seen. Subsequent deep x-ray therapy had no effect in staying the course of the disease.

Present Illness.—About six weeks prior to admission to St. Joseph's Hospital (Case No. 48862) on March 9, 1939, the parents first noted a discharge of pus from the vagina. This persisted and on one or two occasions, the mother noted something protruding from the vagina. This protrusion was not constant; at times it would disappear. The child was taken to several doctors who diagnosed an infection. The discharge persisted and for the past two weeks there has been a small mass persistently projecting from the vagina. The child's appetite has failed markedly. She has lost weight. In the past two weeks the child has had difficulty urinating, having to strain and complaining of pain.

Past History.—The patient was a full-term spontaneous delivery 21 months ago. There were no abnormalities. The child took her formula well and gained steadily. She suffered from repeated "colds" but otherwise gained well and was normal in every respect until the onset of present illness.

Physical Findings.—The child lies in bed appearing pale, feverish and moderately ill. Fulness in lower abdomen with a fixed, firm mass felt in the left lower quadrant. The bladder was moderately distended. Liver and spleen not felt.

Protruding through the vulva was the tip of an irregular cellular mass about 2 cm. in length and 1 cm. in diameter, dark-red and gray in color, firm to the touch, fleshy but not hard. The mass occupied the entire vagina and extended into the right left lower quadrant. On the anterior and posterior aspects of the vulvar portions were several pale, edematous grapelike bodies that could be broken off with the finger. There was no evidence of any cervix and the finger could be swept between the tumor mass and the posterior bladder wall, the latter having an uneven surface as if invaded by the tumor. On catheterization only a few drops of urine were obtained. There was a rather diffuse sanguinopurulent discharge from the vagina.

Biopsy Report.—Microscopic: Nine different pieces were selected for microscopic study. Although they vary slightly in structure, they all are made up of predominately myxomatous tissue. Some areas are fairly cellular and early mitotic figures are seen. In some parts the tissue is slightly fibrous with wide hyalinized areas and showing many small, thickened blood vessels. Two of the larger pieces are partly

surrounded by rather thinned-out, stratified, squamous epithelium. There are also areas showing necrosis and hemorrhage.

Diagnosis.—Myxosarcoma (Sarcoma Botryoides).

Autopsy Report.—Path. No. A-3378. (G. B. Kim.) Body is that of a markedly emaciated, white female child. Rigor mortis has not set in. There is marked generalized pallor. There is slight dependent post-mortem lividity. The skin is wrinkled and there is atrophy of the sub-

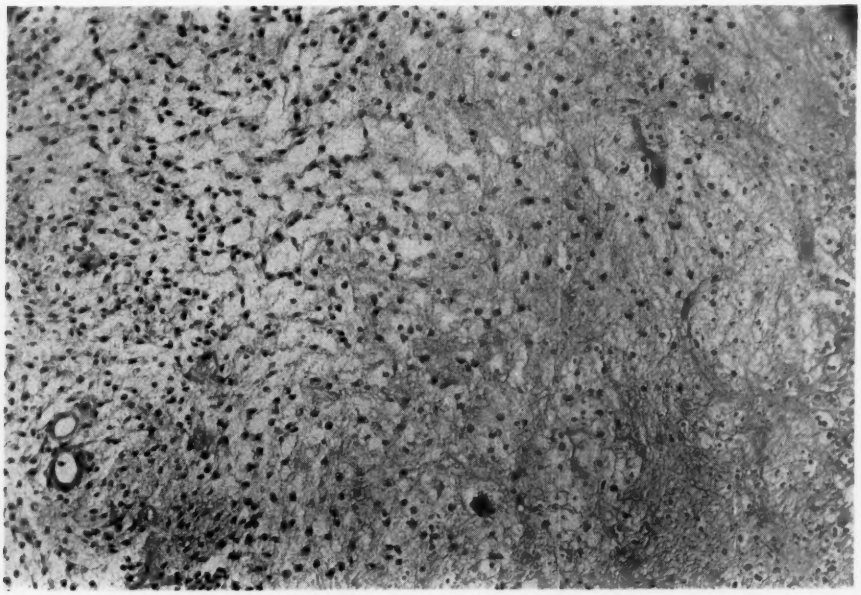

Fig. 1.—Sarcoma Botryoides. Low power photomicrograph (×100).

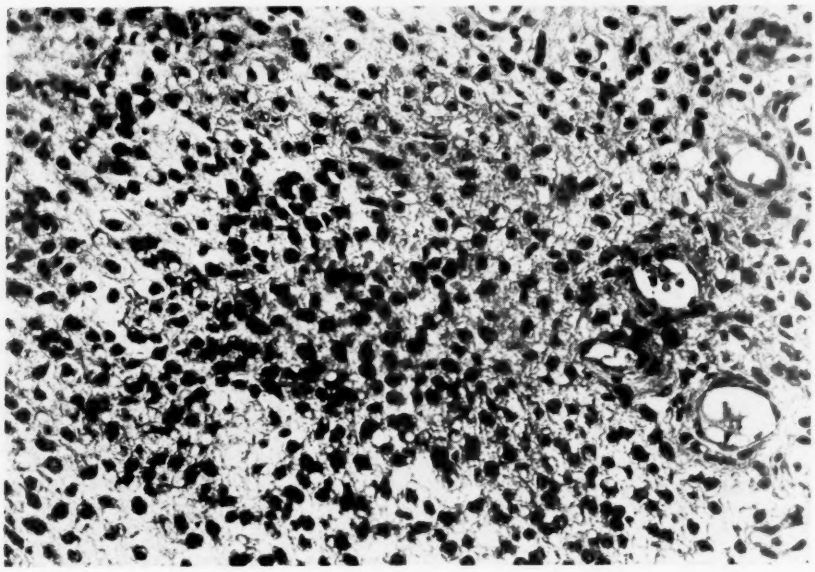

Fig. 2.—Sarcoma Botryoides. High power photomicrograph (×430).

cutaneous fat tissue. Protruding from the vagina, there is a polypoid, hemorrhagic and edematous mass of tissue which on palpation is found to extend into the vagina and is adherent to the lateral vaginal walls. There are no scars, petechiae or icterus. Edema is not noted.

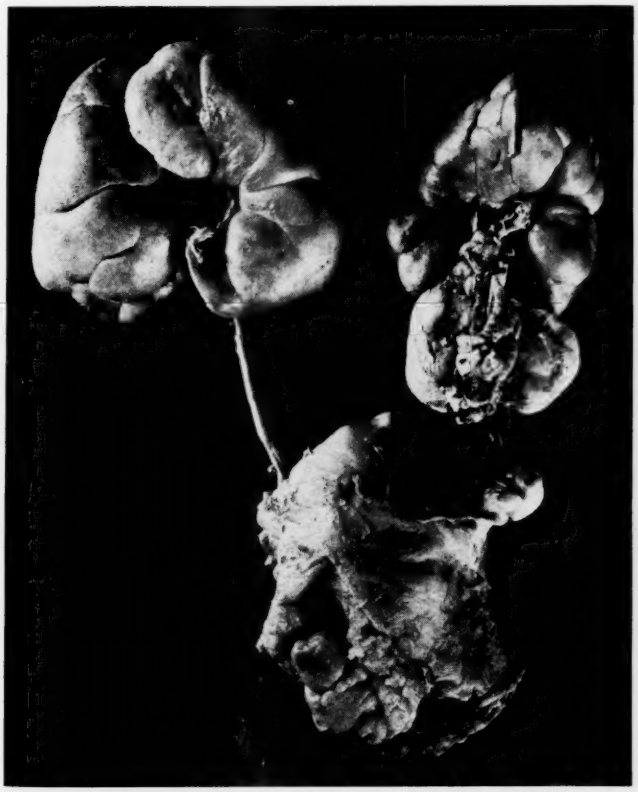

Fig. 3.—Sarcoma Botryoides. Anterior aspect from above downward.

Abdomen.—The skin over the lower abdomen is pigmented, light-brown in color. Distention is more marked in the lower half. The panniculus adiposus is very thin and there is relaxation of the abdominal musculature. The peritoneal cavity contains no free fluid. The peritoneum is smooth and glistening. The greater omentum is adherent to the dome of the bladder. Upon separating it a small amount of purulent exudate is exposed, which is bounded by the omentum superiorly, the dome of the bladder distally and several loops of small intestine posteriorly. There is a perforation in the dome of the urinary bladder from which purulent material exudes and which leads directly into the abscess cavity as described. The liver and spleen are smooth. The liver extends 2 fingerbreadths below the costal margin. The spleen is hidden under the costal margin. The small and large intestines are both moderately distended. The pelvis, after exposure of the abscess cavity, is seen to be filled by a distended bladder and an enlarged uterus. There are several bands of firm, fibrous adhesions between the uterus, bladder and pelvic walls. The uterus is adherent to the bladder and the anterior and posterior cul-de-sacs are obliterated.

Liver.—The organ appears somewhat enlarged, firm, and the capsule is smooth and glistening. On section, it is yellow-brown in color. The cut surface presents a parboiled appearance. The lobular markings are not distinct. The portal fields are seen as pin dots, the central zones are not readily distinguishable. The hepatic and portal vessels are normal. The gall bladder and bile ducts are not noteworthy.

Spleen.—The organ is moderately firm and the capsule smooth and glistening. On section the Malpighian follicles are seen as pinhead-sized grayish areas surrounded by the deep brick-red pulp. The pulp does not scrape. The splenic vessels are normal.

Fig. 4.—Sarcoma Botryoides showing kidneys, lymph nodes, ureters. Posterior aspect with uterus open.

Pancreas.—The lobular markings are distinct. The organ is pale and firm.

Adrenals.—The cortex is of normal width, pale yellow and well demarcated from the gray medulla.

Genitourinary Tract.—Both kidneys are enlarged. The perinephric fat tissue is somewhat edematous and firm. The capsules strip readily, revealing a somewhat finely, granular surface with accentuated fetal lobular markings. Both kidneys are swollen and reddish-gray in color. The cortex is widened and shows scattered hemorrhagic or gray streaks coursing upward from the medulla. They are linear in character and merge with the gray corticomedullary zone. The cortex is moderately well differentiated from the medulla. The medullary pyramids are flattened and the calices dilated. The pelves are markedly dilated on

both sides, as are both ureters. A large amount of urine is present in the pelves and ureters on both sides. The mucosa of the calices, pelves and ureters is injected and granular. The dilatation is more marked on the right side. As far as the ureters can be traced to the bladder, they are seen to be dilated.

The bladder is firmly adherent to the anterior vaginal wall and uterus with obliteration of the anterior cul-de-sac. The whole forms a large tumor mass which is removed from the pelvis with some difficulty. The dome of the bladder leads to the abscess described above. The bladder is enlarged and occupied by a tumor mass which invades the anterior and lateral vaginal walls, the cervix, body of the uterus and projects along the vaginal walls to the labia minora, adherent to these on both sides and then projects through the vaginal orifice. The tumor mass is semisoft and composed of lobules of gray-white, edematous appearing tissue which is quite friable and granular. The lobules vary in size from 5 to 20 mm. in diameter, project through the urethral and vaginal orifices in polypoid fashion resembling large bunches of grapes. The base of the polypi is broad, the tips are hemorrhagic. The bladder is filled with tumor and a small amount of purulent exudate. The fornices of the vagina are invaded by a tumor which extends for a short distance down the posterior vaginal wall and all along the anterior vaginal wall. The cervix is patulous and filled by tumor which can be traced along the endometrial cavity. The uterus is enlarged but there does not appear to be any invasion of the myometrium. The tubes and ovaries on both sides are plastered to the pelvic wall by firm fibrous adhesions. The tubes are both dilated, the lumina widely patent and filled with clear fluid. The mucosal folds are flattened. The fimbriated ends are sealed by adhesions. The ovaries are small and undeveloped.

Lymph Nodes.—The left renal hilus contains a large, firm lymph node which is discrete, enlarged to walnut size and well encapsulated. On section, the normal lymphatic structure is gone and is replaced by a yellow, firm tumor tissue. There is no other gross evidence of lymph node involvement elsewhere in the body.

Chest.—Due to the limitations of the autopsy permission, a complete chest inspection was not possible. The pleural cavities contained no free fluid and the pleurae were smooth and glistening. The lungs were soft, well aerated, pinkish in color and on section showed normal lobular architecture. The pericardial cavity contained about 5 c.c. of amber-colored, clear fluid and the pericardium was smooth and glistening. The cardiac chambers were neither dilated nor hypertrophied. The valves and endocardium were normal. The myocardium was firm and brownish-red. The coronary ostia and lumina were patent. The aorta was elastic and smooth. The venae cavae were negative. There were no enlarged lymph nodes.

Anatomical Diagnosis.—

1. Sarcoma botryoides with invasion of bladder, cervix, vagina and uterus.
2. Perforation of fundus of bladder by tumor with localized pelvic abscess.
3. Metastasis to left renal hilus lymph node.
4. Tumor obstruction of both ureters with bilateral hydroureter, hydronephrosis and ascending pyelonephritis.
5. Bilateral hydrosalpinx.

6. Parenchymatous degeneration of heart and liver.
7. Extreme cachexia.

Microscopic.—Examination shows rhabdomyosarcoma arising in striated muscle and situated in the uterine wall and arising probably in a teratomatous group from the bladder or uterine wall. (Drs. Gerber and De Ostenay.)

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99 PARK AVENUE

MYELOGENOUS LEUCEMIA COMPLICATING PREGNANCY*

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EVERY publication on the subject contains the statement: "leucemia is rare in pregnancy," but there is very little discussion of the reasons why.

It is certainly extraordinary that in a disease causing 3,500 deaths annually in the United States alone,[1] and with a steadily increasing incidence,[2] there should be only 79 cases[3] complicated by pregnancy, reported in the entire medical literature.

Are leucemic women sterile? Or/and is there some factor, hormonal perhaps, in pregnancy, which inhibits the development of leucemia? Over 50 per cent of chronic cases reported had leucemia longer than one year before conception occurred;[3] at least two became pregnant several times in the course of the disease;[4, 5] one case became pregnant after x-ray sterilization because of the leucemia.[6] These cases certainly are not evidence of sterility.

The following is another case in point:

The patient, Mrs. B. T., 22 years old, was first seen on December 14, 1942. She had been married three months and had a two months' amenorrhea, her last menstrual period having begun on October 18, 1942.

She appeared as an obese, rather flabby and dull young woman. She complained of slight headache and morning nausea for the past month. Her past history was negative except for the usual childhood diseases. Her tonsils had been removed at the age of 10. Menstrual periods, onset at age 13, were regular, every 28 days, lasting four or five days.

Her weight was noted as 168½ pounds, blood pressure 110/70, hemoglobin 75 per cent, urinalysis negative except for a faint trace of albumin, blood Wassermann negative. The physical examination revealed no abnormality except overweight and slight pallor of mucous membranes. The pelvic examination revealed an early pregnancy, approximately six weeks. The patient was instructed to report in one week. She did not return, however, until two months later. At that time she still complained of headache and nausea. She had made an attempt to follow dietary instructions, had taken her vitamins and iron; her weight was 165¼ pounds. The gestation appeared to be progressing normally.

Two weeks later, February 21, 1943, she reported having had abdominal pains for three days, and that morning having been seized with a sudden aggravation of the pain accompanied by vomiting. She was seen shortly after at the Woman's Hospital. Temperature 98.6, pulse 80, respirations 20, blood pressure 94/60, slight pallor was noted. No abdominal tenderness was demonstrable, and no masses, outside of the enlarged uterus, but the patient gave a history of acute colicky pain in the left hypochondrium, lasting up to her admission to the hospital.

*Read at a meeting of the Philadelphia Obstetrical Society, March 2, 1944.

A routine blood count taken on admission, showed 68 per cent hemoglobin, 3,400,000 R.B.C. and 106,250 W.B.C. with 24 segmented, 32 stabs, 6 juveniles, 5 lymphocytes and 32 myelocytes. The urine was essentially negative.

During the five days' stay in the hospital, the W.B.C. ranged from 106,250 to 122,250 with myelocytes ranging from 22 to 37 per cent. An x-ray study showed no enlargement of the liver or spleen and no abnormality of the bones. She was discharged with a diagnosis of chronic myelogenous leucemia complicating pregnancy, and given Fowler's solution, initial dose three minims, t.i.d., increasing to fifteen minims t.i.d.

This medication had to be discontinued in three weeks due to the occurrence of diarrhea. The W.B.C. had meanwhile dropped to 88,000. In April, she had a respiratory infection, following which she complained of pain in the left loin radiating to the left thigh. The W.B.C. had risen to 180,000, the urine negative. She was put back on Fowler's solution, Feosol and vitamin capsules—the W.B.C. again dropped to 88,000, the spleen was palpable 1 cm. below rib margin. In her thirty-fourth week of gestation she had another attack of severe abdominal pain, which required morphine for relief. At this time the spleen appeared enlarged and extremely tender, extending 4 cm. below the costal margin. There was marked abdominal distention although the uterine fundus was only 2 cm. above the umbilicus. Fetal movements and heart sounds were normal, however, the fetus lying in right occipitoposterior, the vertex unengaged. Temperature, pulse, blood pressure and urine were normal. The blood count showed 68 per cent hemoglobin, 3,600,000 R.B.C., 126,500 W.B.C. with 23 per cent myelocytes: platelet count 242,000, prothrombin, coagulation and bleeding time normal, Rh factor positive. Medical induction of labor was attempted at this time without success. X-ray treatment was then instituted and given every other day during the period between June 12, and June 21. The areas irradiated were the femora, anterior and posterior, the chest anterior and posterior, 75r. each time. After the fifth treatment, the W.B.C. was 69,500, with 26 per cent myelocytes.

On July 19, 1943, in the fortieth week of gestation, the patient was admitted to the hospital with ruptured membranes, and light, irregular pains. Fetus in R.O.P., fetal heart sounds good, vertex unengaged. Labor progressed very slowly, and lasted 50 hours in all. There was marked abdominal distention throughout the labor and for several days of puerperium. The patient's pelvis was of the funnel type, and the vagina small with a short perineum. The fetal head was arrested in midpelvis and delivery was finally effected with Dewees forceps. Right mediolateral episiotomy was done, but there occurred a third-degree laceration of the perineum. The patient received seconal and scopolamine during the first stage of labor, ether anesthesia, pituitrin and ergotrate at the end of the third stage. Absence of excessive bleeding was noted here as has been noted by several others, and the perineal repair healed perfectly.

The infant, male, 7 pounds, 2 ounces, appeared to be in fair condition at birth. A large caput formation was evident, the cry rather feeble. The second day postnatal, there appeared evidence of cerebral irritation, but this responded well to treatment. A fracture of the right clavicle was demonstrated by x-ray. On discharge, he appeared to be

in good condition, weighing 7 pounds, 11½ ounces. The blood count showed no abnormality at any time.

Even though there was no excessive loss of blood during labor, the entire blood picture showed such deterioration immediately after, that a transfusion of 500 c.c. whole blood was given. The W.B.C. on admission was high, 276,500, with 29 per cent myelocytes, but at the end of labor reached its highest, 323,000, with 32 per cent myelocytes. X-ray treatment was resumed on July 30, 1943. At that time the spleen was noted as being very much enlarged, displacing the splenic flexure of the colon downward and reaching to 3 cm. above the iliac crest. She received four treatments, two to the spleen, two to the femora, but after the last treatment, there was such a sudden drop in the white count (to 12,600) that she was again transfused.

When discharged on August 10, 1943, the patient was in good condition, the only physical abnormality being the enlarged spleen; W.B.C. 10,800, myelocytes 31 per cent. She felt fine and had no complaints until November when she reported pain in the left supraclavicular and shoulder regions. There were no nodes palpable in those areas. She had been taking 45 minims of Fowler's solution daily, but the W.B.C. had been steadily rising and had reached 199,000 with 33 per cent myelocytes. She refused further x-ray treatment, however, and failed to report for her next appointment.

Comment

It does not seem to be the prevailing practice to take a complete blood count early in ante-partum care. Some obstetricians do not do any at all, some take a complete blood count in the last trimester. In the printed forms used in many prenatal clinics, there is space for hemoglobin estimation only.

In chronic leucemia, the symptoms are often vague and confusing. Without blood studies, one would hardly have suspected our patient of being affected by such a serious disease.

How serious is the disease, is well established. How much it is aggravated by pregnancy, is a controversial point.

Kosmak[7] states that the prognosis in the pregnant is undoubtedly worse than in the nonpregnant.

Moloney and Hefferman[8] feel that leucemia is uninfluenced by gestation.

Grier and Richter[9] found exacerbation to be the rule.

To McGoldrick and Lapp[3] it seems that the course of leucemia is not greatly, if at all, affected by pregnancy.

More controversial still is the method of treatment.

Grier's[9] oft quoted statement that, "only two men have seen as many as three cases of leucemia associated with pregnancy," certainly explains why such diametrically opposite stands are taken by different clinicians, particularly in reference to irradiation and to the interruption of pregnancy and the sterilization of the patient.

The conflict of opinion on the latter is obviously due to meager statistics; on the subject of x-ray therapy, those[3, 10] who decry its use in the pregnant, surprisingly, appear to ignore the fact that the authors[11-13] quoted on the undesirable effects of irradiation, are referring specifically to pelvic, or to fetal irradiation.

Summary

1. A case of chronic myelogenous leucemia complicating pregnancy, treated with arsenic and with x-ray, and delivered of an apparently normal child has been presented.

2. Aggravation of the disease was noted as the pregnancy advanced.

3. Potassium arsenite, although at first effective, later was insufficient to control the symptoms.

4. Irradiation appeared to check the leucocytosis and the pain.

5. The importance of having complete blood counts early in pregnancy is demonstrated, also the necessity of gathering more data for the proper evaluation of methods of treatment in this grave complication of pregnancy.

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1209 SOUTH BROAD STREET

EMBRYONIC CARCINOMA OF OVARY IN A GIRL 13 YEARS OF AGE*

SAMUEL GOLDSTEIN, M.D., F.A.C.S., PITTSBURGH, PA.

(From the Montefiore Hospital)

OVARIAN cancer is comparatively rare in childhood. Kamniker[1] in 1939, reported that out of a total of 2,277 cases of genital cancer seen in the University Woman's Clinic in Vienna, between 1921 and 1933, there were only 157 cases of ovarian cancer, among which were only two cases in patients under 20 years of age, and eight between 21 and 30 years of age. W. Warren Sager[2] reports that out of 42,864 admissions in the ten years between 1928 and 1938 to the Children's Hospital in Washington, D. C., there was only one ovarian cancer, it being in a girl of nine years of age. Gardner,[3] quoted by Sager reported cancer of the ovary in a patient of six years of age. The youngest patient with cancer of the ovary that I found on record was by Forsthius in a girl of three years of age with a complex teratoma of the ovary. Winternitz reported a cystic embryoma of the right ovary in a girl of six years of age. In 1919, H. M. Gerson,[4] reported in the Lancet, a case of papillary cancer of the left ovary in a girl of nine years of age. In 1909, Lahey and Haythorn[5] reported a case of solid cancer of ovary in a girl of eleven years of age.

Case Report

Miss N. S. (0-1130) was admitted to the Montefiore Hospital on March 2, 1942. She gave a history of being raped in July, 1941. She then missed the August period. In September, six weeks after the attack, she began to bleed. Since that time she has had irregular staining. The only other complaint, in addition to this irregular staining was the gradual enlargement of the abdomen.

Abdominal examination revealed a large symmetrical tumor, extending to about one finger above the umbilicus.

Pelvic examination revealed a hymen that was not intact. A large semicystic tumor extended to about one finger above the umbilicus, probably an ovarian cyst. A smaller mass, the size of a grapefruit was palpated to the left of this large mass, which was thought to be an enlarged uterus. The cervix was normal.

Laboratory Studies.—

1. Friedman pregnancy test was *positive* on two separate tests.
2. X-ray of abdomen, revealed *no* fetal skeleton.
3. Blood count and urine studies showed no abnormality.
4. Blood Wassermann was negative.

A preoperative diagnosis of ovarian cyst with an enlarged uterus was made.

*Presented at a meeting of the Pittsburgh Gynecological and Obstetrical Society, Feb. 7, 1944.

Patient was operated upon March 7, 1942. On opening the peritoneal cavity, a large semicystic mass, the size of a large football, well encapsulated, arising from the left ovary was found. Another mass, the size of a large orange, more solid than the larger mass, and attached by a small pedicle was also present which was densely adherent to the sigmoid and to the omentum. The right tube, ovary, and uterus appeared normal. Palpation of the liver revealed no metastases. A bilateral salpingo-oophorectomy and a hysterectomy were performed.

The patient made an uneventful recovery and was discharged from the hospital on March 22, 1942, three weeks after admission. Deep x-ray therapy was started before the patient left the hospital.

Fig. 1.—Gross specimen of the left adnexal mass, the uterus and normal right tube and ovary.

On September 9, 1942, six months later, the patient was admitted to the hospital with ascites and generalized metastases. She died two days later.

Pathological Report.—(Dr. K. Y. Yardumian.) The specimen consisted of a uterus, two tubes, a large ovarian mass, and ovary. The ovarian mass weighed 12 pounds, cystic in character, well encapsulated. There was another mass the size of an orange attached to the original mass by a pedicle. On sectioning, the large mass showed numerous cysts filled with mucoid substance. In between the cysts there were solid areas with yellowish discoloration. The smaller mass had occasional cysts, mostly solid, sulfury-yellow with multiple hemorrhagic areas. It was very soft and friable and had the gross appearance of malignancy.

The uterus was infantile in size. The endometrium was smooth. No evidence of neoplasm. The tubes showed nothing remarkable. The

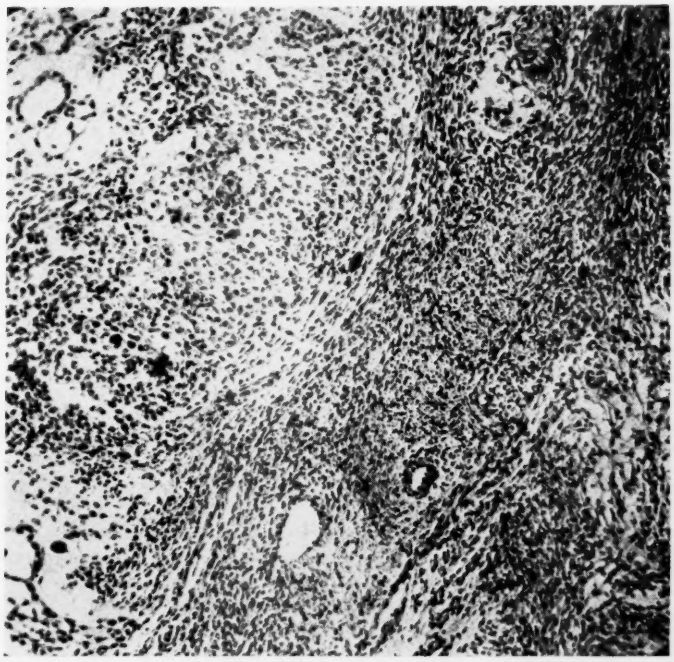

Fig. 2.—Low power magnification (×100), hematoxylin and eosin stain showing a very cellular structure with loose stroma.

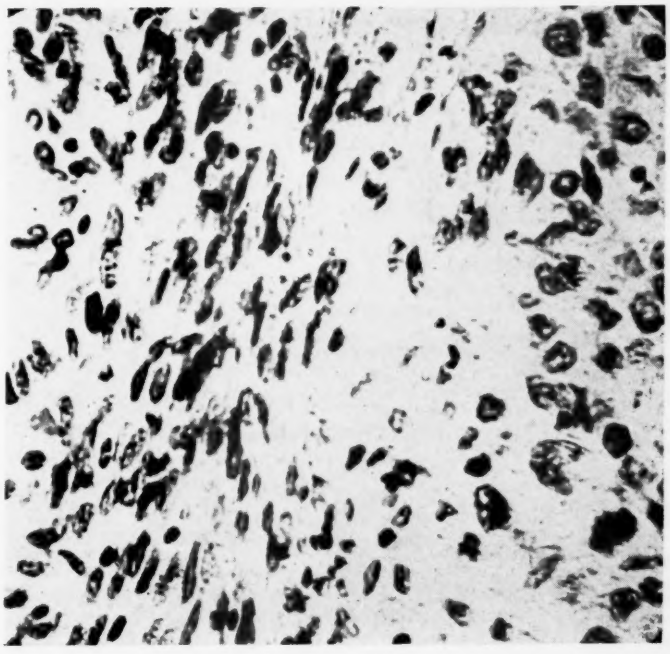

Fig. 3.—High power magnification (×400), hematoxylin and eosin stain showing undifferentiated cells, mostly pleomorphic. There are numerous atypical mitotic figures. The cells are widely separated by mucoid stroma.

opposite ovary was normal in size and shape, showing numerous follicular cysts.

Sections from the ovarian tumor showed spindle-cell stroma with islands of undifferentiated epithelial cells, pleomorphic in type with mucoid stroma. The blood vessels had very thin walls surrounded by tumor cells. Other portions of the tumor showed glandular structure with mucoid degeneration lined by cuboidal epithelial cells.

Sections of the opposite ovary did not show any involvement with neoplastic changes.

The endometrium also showed normal histologic structure.

Diagnosis.—Embryonic carcinoma, pseudomucinous cyst adenoma of ovary.

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4136 Jenkins Arcade

FETAL DYSTOCIA FROM A FACE PRESENTATION WITH FORELYING ELBOW

JOHN JOSEPH GILL, M.D., CHICAGO, ILL.

(From the Illinois Central Hospital)

THE following is a case report of a mento-left-anterior position, locked in the grasp of the forelying left elbow, presenting at the pelvic inlet.

This particular dystocia, caused by a malposition of the fetus during a cephalic engagement, is considered of sufficient rarity to merit recording. For that reason I wish to report this case, with the consent of Dr. Ross S. Lang, by whom I was consulted.

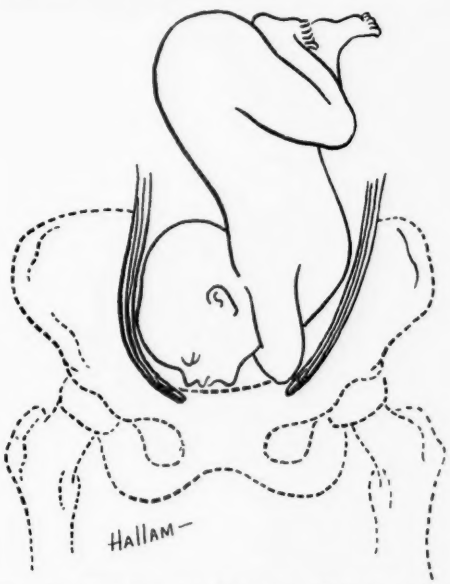

Fig. 1.—Showing relations of child to pelvis.

Mrs. S., aged 21, expected the birth of her second baby on August 10. There was no cephalopelvic disproportion, her prenatal care had been adequate, the past health record was exceptionally good.

On July 29, at 6 P.M., the labor pains started, two hours later she entered the hospital. The pains continued with increasing strength and frequency. After twenty-four hours of labor, the membranes were intact and rectal examination was unsatisfactory.

On July 30, at 6 P.M., a vaginal examination was made. The cervix was found to be completely dilated, the membranes were ruptured artificially, disclosing the reason for the labor without progress. The

forelying left elbow presented under the fetal chin, with the left hand extending over the right shoulder, fixing the head in extreme extention, to the right side of the mother's pelvis, the face toward the left and slightly anterior.

Treatment consisted in releasing the impacted left arm, flexing the head and manually manipulating the presenting parts into an occipito-right-anterior, in which position, delivery terminated in the spontaneous birth of a living male, weighing seven and one-quarter pounds, at 7:25 P.M.

The infant's left arm was swollen and blue from axilla to wrist, for several days; recovery was complete, mother and baby were discharged in good condition on August 8.

A SIMPLE UMBILICAL CORD CLAMP

HARRY S. FIST, M.D., LOS ANGELES, CALIF.

THE cord clamp here illustrated is placed on the cord quickly, prevents bleeding, and may be removed and resterilized when the cord stump has dropped off. It is made from an ordinary safety pin by making two bends in the catch end and pressing both sides of the coil spring end together. The extra pin length is cut off, leaving the tip dull and safer for gloves.

Fig. 1.—Cord clamp.

To apply, slip the open clamp over the cord at about one-fourth inch from the abdomen of the baby and, using the thumb, press the pin to the lock slowly so that the Wharton's jelly will ooze out of the way without cutting the blood vessels. A hemostat may now be placed about one-fourth inch from the clamp and the cord cut between the clamp and hemostat. Antiseptic dressings are applied and the clamp left in position to remain until separation of the cord stump.

This clamp is cheap, easily used, will not open or drop off; and may be easily and quickly made by anyone who has a supply of safety pins, a pair of small pliers and a little patience.

1930 WILSHIRE BOULEVARD

Department of Reviews and Abstracts

Selected Abstracts

Anesthesia, Analgesia, etc.

Carengelo, John: Continuous Caudal Anesthesia in Obstetrics, South, M. J. 37: 80, 1944.

Continuous caudal anesthesia with 1½ per cent metycaine was used by the author on 61 patients. He prepares the patient with a small dose of a barbiturate, and gives a cleansing enema. The technique employed was that described by Hingson and Edwards: a steel malleable needle inserted along the roof of the sacrum and connected to a 2-way syringe to facilitate the administration of the anesthetic solution. Potential errors and complications such as subcutaneous instead of extradural insertion of the needle, intravenous injection, subarachnoid injection, broken needles, unilateral anesthesia, and low back pain are mentioned. Contraindications are placenta previa, uterine inertia, hysteria, infections near the sacral hiatus, dystocia, and anatomic defects in the sacral hiatus. Average metycaine dose for all patients was 1.4 grams, the largest dose to a single patient during her labor was 6 grams. Forceps, version and cesarean section were performed without supplementary anesthesia. Post-partum blood loss was minimal. No complications were encountered in this series other than bladder atony. The author emphasizes the importance of observing the bladder during labor as the patient's impulse to void is lost while under anesthesia and overdistention may occur.

WILLIAM BICKERS.

Volpitto, Perry P., Woodbury, Robert A., Abreu, Benedict E., and Torpin, Richard: Continuous Caudal Analgesia in Normal and Complicated Labor: Report of a Death, South. M. J. 37: 83, 1944.

Metycaine and Procaine in 1 per cent or 1½ per cent solutions were administered through a #18 rigid steel needle into the caudal canal of 75 patients who were in active labor. Breech deliveries, forceps, craniotomies, a placenta previa, abruptio, and twin delivery were managed under caudal. Throughout labor in 4 patients, the intrauterine pressures were recorded optically according to Woodbury's technique. The effects of caudal analgesia on uterine pressure are shown by tracings. Introduction of the needle into the sacral canal causes increased pressure within the uterus, this tension falls when the analgesic drug becomes effective. The rate and amplitude of contractions diminish in the presence of caudal analgesia. Complete pain relief was accomplished in 51 of the 75 patients, in two patients the needle could not be introduced into the canal, 21 patients had partial relief. Two patients developed infections at the needle site, vomiting occurred in ¼, and there were 4 infant deaths. One maternal death occurred 25 minutes after administration of 30 c.c. of 1½ per cent metycaine. This patient was a negress, obese (200 pounds), luetic, with pitting edema of the lower extremities. Taking the usual precautions to be sure that the needle was properly placed, the solution was injected and 20 minutes later the blood pressure was only slightly below its original level. Five minutes later she collapsed and could not be resuscitated. Post mortem revealed

only generalized passive congestion and evidence of sick-cell anemia in the bone marrow. No metycaine could be recovered from careful study of the spinal fluid. The baby was rescued by prompt delivery per vaginam. Two rather severe infections occurred in this series, both in obese patients: they were cured by x-ray and sulfathiazole therapy.

WILLIAM BICKERS.

Endocrinology

Harding, Floyd E.: The Oral Treatment of Ovarian Deficiency With Conjugated Estrogens-Equine, West. J. Surg. 52: 31, 1944.

A comparison of the conjugated estrogens in a dose tablet of 1.25 mg. of the water-soluble conjugated form expressed as sodium estrone sulfate (Premarin) was made with estradiol benzoate, diethylstilbestrol dipropionate, and estrone. Various ovarian deficiency states were treated such as surgical menopause, the physiologic menopause, hypo-ovarian amenorrhea, vaginal atrophy, and senility. Marked improvement in the general well-being as well as relief of the hot flushes was noted in the menopause group. The amenorrhea group improved in their mental and physical aspects. The author believes that one tablet of this mixed conjugated hormone is more effective than 4,000 I.U. of estrone hypodermically. Vaginal smears could be cornified by oral administration of this hormone. No evidence of toxicity such as that seen in stilbestrol therapy was noted. Uterine bleeding was induced in certain of the menopause cases and delay of the menses was noted particularly in those prone to a hypomenorrhea.

WILLIAM BICKERS.

Novak, E.: Limitations and Possible Hazards of Endocrine Treatment in Gynecology (Editorial), Am. J. Surg. 56: 523, 1942.

Although fully cognizant of the comparatively recent tremendous advances in the field of endocrinology as it applies to the female reproductive mechanism, the author carefully appraises the status of endocrinologic therapeusis as it is practiced at the present time. He calls particular attention to the marked discrepancies that exist between the results obtained by animal experimentation and those obtained in the human female. He suggests that a more critical attitude on the part of both laboratory workers and clinicians in formulating their observations will eliminate the tendency to "mislead the uninformed reader and perhaps to disgust those better qualified to detect the fallacies with which they so often abound." He stresses the following points:

1. Since both ovarian hormones, estrogen and progesterone, are now readily available in pure form, there is no excuse for the use of such preparations as ovarian substance, ovarian residue, or corpus luteum.

2. Estrogenic substances do not stimulate the ovary but are only substitutional in the treatment of amenorrhea. They cannot influence cases of sterility.

3. The preparation, stilbestrol, is valuable, especially in the treatment of menopausal symptoms, but should be handled circumspectly.

4. Although there is no acceptable evidence that the estrogenic substances are carcinogenic in the human, the wise clinician will avoid unnecessarily large dosage in patients harboring a precancerous type of lesion or in those in whom a predisposition toward cancer may be suspected.

5. No efficacious gonadotropic principle as applied to the human female is as yet available. Clinical results with preparations of this group have been disappointing.

6. The indiscriminate use of the equine gonadotropic principle in the treatment of sterility is condemned.

7. Treatment of dysmenorrhea and functional bleeding with various hormones is indicated. However, other measures should not be excluded.

8. Androgenic hormone therapy in certain cases of functional bleeding and primary dysmenorrhea is justifiable as is shown by the results obtained. To prevent the troublesome masculinizing symptoms which frequently appear, smaller dosage is recommended, especially in patients who show a tendency toward hypertrichosis.

FRANK SPIELMAN.

Endometriosis

Hurd, R. A.: Some Observations on Endometriosis, Am. J. Surg. 53: 61, 1941.

An analysis of 135 cases of endometriosis occurring at the Woman's Hospital, New York, during the past decade is presented. The author believes very strongly that the transtubal implantation theory of Sampson is the most satisfactory as to etiology, and that it should receive the general acceptance of the profession. In most cases endometriosis is associated with, or appears as a complication of some inflammatory or neoplastic condition of the uterus or its appendages, or is the factor responsible for the adhesions seen in fixed retroversion.

The symptoms of endometriosis were rarely typical in this series. They consisted in abdominal pain, backache, and menstrual disturbances, just as in patients manifesting tumors, inflammatory disease or malposition of the pelvic viscera. Dysmenorrhea, which has been stressed by several authors as almost pathognomonic of the disease, was the sole or outstanding complaint of relatively few of the cases here observed, although a majority of patients stated that their symptoms were aggravated at the time of menstruation. Forty per cent of the cases had had previous gynecologic operations, either by laparotomy or from below, and the ratio of nulligravida to parous women was about 5 to 4.

In treatment, operation is the method of choice although radiotherapy may also be used. The author tends to favor radical excision of the pelvic viscera when the involvement is marked. In young women more conservative procedures may be performed especially where preservation of the menstrual and childbearing functions are desirable.

FRANK SPIELMAN.

Gynecology

Phaneuf, Louis E., Heffernan, Roy J., and Kasdon, S. Charles.: Functional Urinary Incontinence in Women, New England J. Med. **229:** 743, 1943.

The authors report a series of twenty-three cases operated upon by the Kennedy technique. Three drawings help to illustrate and to clarify the essential points of the operation.

Either marked improvement or complete late recovery of the bladder function was obtained in eighteen cases, or ninety-one per cent.

The two failures which occurred are presented, and possible causes for failure are discussed.

JAMES P. MARR.

Schwartz, F. L.: Uterine Prolapse, Am. J. Surg. 53: 111, 1941.

By utilizing x-ray in conjunction with a Hyams cannula introduced into the cervix, the author attempts to correlate symptoms referred to the pelvis and ostensibly due to prolapse, with the degree of actual prolapse present. This is accomplished by taking x-ray plates with the cannula in place pushing the cervix high into the pelvic cavity, and again after the cervix has been pulled down by means

of a tenaculum devised by the author. Measuring from a fixed point on the symphysis pubis, the degree of excursion of the cervix by this technique determines the degree of prolapse. In a series of 25 cases studied, the average mobility in the group without symptoms was 2.6 cm. and the average "low" above the symphysis, 5.5 cm. In the group with symptoms, the average mobility was 5 cm. and the "low" point above the symphysis, 1.2 cm. The author concludes that a "low" point less than 3.5 cm. together with mobility greater than 4 cm. indicates uterine relaxation of sufficient degree to be capable of causing symptoms. Uterosalpingography may be utilized while performing this procedure if additional information regarding the uterus and adnexa is desired.

FRANK SPIELMAN.

Harrell, W. B.: The Pelvioscopic Method of Uterine Suspension, Am. J. Surg. **62:** 149, 1943.

A method of performing a Gilliam suspension of the uterus using the "pelvioscope" is described. The instrument is a modified endoscope whose barrel is 11 cm. in length and 1 cm. in diameter, and whose obturator has a tapering triangular cutting point extending about 4 cm. below the sheath. Light is obtained by means of a small electric light which is fitted to the cylinder. A dull hook about 18 cm. long is used to grasp the round ligaments in performing the operation. The instrument is introduced into the peritoneal cavity through an incision 1 cm. long on each side of the midline. The obturator is then removed, the round ligaments identified and brought into the wounds to be sutured above the fascia. The author believes this procedure "to have moderate usefulness in that it may be performed successfully on those cases of uncomplicated retroversion and retroflexion that appear to be producing symptoms." The patients may become ambulatory the first postoperative day and the period of hospitalization reduced to one or two days.

FRANK SPIELMAN.

Jeffreys, E. M., and Graffagnino, Peter: Incidence, Treatment and Prevention of Hydatid Mole and Chorionepithelioma, West. J. Surg. **52:** 29, 1944.

During a ten-year period there was an incidence of 1 hydatid mole to every 3,049 pregnancies. In general the symptoms were bleeding, painful contractions, passage of vesicles, nausea, headache, and dizziness. Two patients had recurrent moles. About 5 per cent of cases with hydatid mole will develop chorionepithelioma; hysterectomy on moles of questionable malignancy will reduce the incidence of malignant degeneration. The author quotes Hertig to the effect that mole is much more common than generally thought, occurring often as a small area on the placenta in spontaneous abortions. About 50 per cent of spontaneous abortions are the result of defective ova and about 60 per cent of these have shown some hydatid change in the placenta. To prevent malignant or hydatid degeneration of placental tissue following abortion, the author recommends dilatation and curettage on all abortions of 3 months' gestation or less. Treatment of hydatid mole consists of thorough curettage with careful study of the scrapings. Monthly Friedman tests should be done and a persistent positive is indication for radical surgery. The frequency of hydatid change in spontaneously aborting ova contraindicates the enthusiastic use of progesterone to prevent abortion. In the study of pathologic material, it must always be remembered that trophoblastic tissue is normally proliferative and invasive, and is frequently borne to the lungs following delivery, and this must not be confused with the metastasis of a malignant chorionepithelioma.

WILLIAM BICKERS.

Boyce, Frederick F.: The Diagnostic Confusion Between Acute Appendicitis and Pelvic Inflammatory Disease, New Orleans M. & S. J. **96**: 303, 1944.

Difficulties in the differential diagnosis between acute appendicitis and acute pelvic inflammatory disease have been intensively studied. The author has analyzed 60 cases with acute pelvic inflammation who were operated upon with the diagnosis of acute appendicitis, and he has studied 46 cases of acute appendicitis which were mistakenly diagnosed as inflammatory disease and operation was therefore postponed. In the first group, the unnecessary emergency operations resulted in no deaths, while in the second group, the error in diagnosis was the cause of 3 deaths. Because the patient has inflammatory disease does not mean that the patient cannot have acute appendicitis as well. Right-sided pain as the first symptoms suggests appendicitis but many of the inflammatory cases had a similar history. Pain arousing the patient from her sleep is more typical of appendicitis. Coincidence of pain with the onset of vaginal bleeding was the same in both groups. Dysuria is much more common with inflammatory disease but does occasionally present itself as a symptom in appendicitis. Chills are much more common in the former. The temperature, leucocyte count, and sedimentation time are not helpful. Backache is much more typical of inflammatory disease and in its absence the author hesitates to make a diagnosis of that disease. In summary, the author emphasizes that acute appendicitis is a complex clinical syndrome which may simulate acute inflammatory disease to such a degree as to make differential diagnosis impossible. In such cases the abdomen should be opened and the appendix removed. If an acute inflammatory disease is found, then the peritoneal cavity is sprinkled with sulfanilamide and closed.

WILLIAM BICKERS.

Hardt, H. G., and Seed, L.: The Diagnosis of Torsion of the Pedicle of an Ovarian Cyst, Am. J. Surg. **56**: 598, 1942.

The records of 69 patients with torsion of the pedicle of an ovarian cyst who were operated upon at the Cook County Hospital, Chicago, from 1925 to 1940 inclusive, are reviewed. Sixty-nine per cent of the twisted cysts were of the simple type, including follicular cysts, corpus luteum and hemorrhagic cysts. The various symptoms which aid in diagnosis are discussed, including pain, nausea and vomiting, menstrual irregularities, abdominal tenderness, rigidity, and the presence of a mass. Radiation of pain down the thigh of the affected side is stressed. X-ray may aid in diagnosis by visualizing calcareous deposits in ovarian neoplasms especially dermoids. Where ordinary pelvic examination is unsatisfactory, examination under anesthesia is suggested.

FRANK SPIELMAN.

MacManus, J. E., and Moore, J. A.: The Value of the Fractional Hormonal Tests in the Diagnosis of Hydatidiform Mole, Am. J. Surg. **56**: 669, 1942.

The authors present 2 cases of hydatid mole both of which were diagnosed preoperatively by means of the Aschheim-Zondek and Friedman tests in high dilution. In the first case, positive Friedman tests were obtained with 20 c.c., 0.025 c.c., and 0.001 c.c. of urine. In the second case, the Aschheim-Zondek test was positive in dilutions of 1 to 50, 1 to 100, and 1 to 200. The Friedman test, however, was negative with 0.025 c.c., 0.005 c.c., and 0.001 c.c. No explanation is offered for the negative reaction in the second case.

FRANK SPIELMAN.

McLaughlin, E. F.: Ovarian Lesions Simulating Appendicitis, Am. J. Surg. **57:** 114, 1942.

The ovarian lesions which most frequently give rise to symptoms suggestive of appendicitis are ruptured Graafian follicles, follicle and corpus luteum cysts, and bleeding corpora lutea. A series of 49 cases with ovarian lesions simulating appendicitis were studied. Of these, 21 showed freshly ruptured cysts at operation, 17 showed unruptured cysts, 3 showed both appendicitis and cyst rupture, and 8 were not operated upon. All of the patients were white, an observation which other authors have repeatedly stressed. The average age was about 25 years, and 70 per cent of the women were unmarried.

Differential diagnosis is carefully discussed, especially in relation to acute appendicitis, pelvic appendicitis, and chronic or recurrent appendicitis. At operation partial resection of the ovary was performed in 37 cases, oophorectomy in 3 cases, and salpingo-oophorectomy once. There was no mortality. As the result of careful follow-up, the author concludes that ovarian partial resection will give freedom from furthur symptoms in 82 per cent of cases. He particularly stresses the necessity for operation where appendicitis cannot be ruled out.

FRANK SPIELMAN.

Hochman, S.: A Review of 500 Gynecologic Patients With Urinary Symptoms, Am. J. Surg. **52:** 472, 1941.

As the result of the study by urethroscopy and cystoscopy of 500 gynecologic patients presenting various urinary complaints, the author reaches the following conclusions: Urinary symptoms in the great majority of female patients have their origin in the vesico-urethral junction. The female patient with urinary symptoms should have a meticulous examination of the urethra, bladder neck and bladder. The correction of gynecologic disease and abnormal physiologic changes is frequently followed by alleviation of the urologic symptoms. Dilatation of the urethra is of definite value in the treatment of diseases of the vesico-urethral junction. Hydrotherapy, general hygienic measures and proper sedation should accompany local treatment. The term, "cystitis," so frequently used as a diagnosis to cover urinary symptoms, should be replaced by that applicable to the specific pathology found.

FRANK SPIELMAN.

Castallo, M. A., and Feo, L. G.: Ovarian Hemorrhage, Am. J. Surg. **53:** 82, 1941.

The authors propose the term, "oophorrhagia," to denote bleeding from an ovulatory site severe enough to produce clinical symptoms or signs. They present a study of 28 cases seen at the Jefferson Medical College Hospital from 1930 to 1939 inclusive. Twenty-six of the cases were operated upon at which time the diagnosis was either established or confirmed. The condition was correctly diagnosed in only 5 instances or 17.8 per cent. It is interesting to note that all of the cases occurred in white women although 50 per cent of the patients admitted to the hospital are colored. Sixty-four per cent of the women were nulliparous and more than half were between 15 and 25 years of age. The operative procedures most commonly performed were oophorectomy, salpingo-oophorectomy, or partial resection of the involved ovary. Conservatism at operation is stressed.

FRANK SPIELMAN.

O'Neill, Thomas: Congenital Absence of the Vagina Treated by the Baldwin Technique, Brit. M. J. 4327: 46, December 11, 1943.

Several of the plastic methods of reconstruction of the vagina are mentioned. The author describes a case in which the small bowel was used to make an artificial vagina with a successful result.

WILLIAM BERMAN.

Newborn

Lewis, J. M., Bodansky, Captain O., and Shapiro, L. M.: Regulation of Level of Vitamin A in Blood of Newborn Infants, Am. J. Dis. Child. **66:** 503, 1943.

The authors studied a series of 108 infants throughout the newborn period to determine the cause of the low concentration of vitamin A in the blood during the first three days of life. This deficiency led the authors to believe was due to the failure of the liver to mobilize and store adequate amounts of the vitamin. In as much as no pathologic disorder was produced, the authors did not recommend frequent administration of vitamin A concentrate.

JAMES P. MARR.

Ingraham, Frank D., and Matson, Donald D.: Subdural Hematoma in Infancy, J. Pediat. **24:** 1-38, 1944.

This lesion is most frequently seen during the first six months of life. Trauma during labor or delivery, or head injuries following are nearly always a factor in producing this entity.

At the Children's Hospital during the past six years, the staff together with the neurosurgeon have confirmed the diagnosis by subdural puncture in ninety-eight patients. Ninety-four of these bilateral burr holes were made. Ninety-four craniotomies were performed with an operative mortality of 5.3 per cent and a case mortality of 7.9 per cent. Fifty-seven patients adequately followed for periods ranging from six months to five years of age, disclosed 23 per cent were retarded or grossly deficient, while 77 per cent were not only asymptomatic, but showed normal behavior.

The authors give in considerable detail the signs and symptoms which indicate subdural hematoma and a carefully planned and detailed technique for surgery is outlined.

Favorable results led the authors to urge the general practitioner, the obstetrician and pediatrician to diligently seek for more such cases, as the frequency with which subdural hematoma is found depends on the intensity for its search.

JAMES P. MARR.

Eichwald, E. J.: Case of an Omental Cyst in a Three Weeks' Old Female Causing Fatal Ileus, Am. J. Surg. **53:** 181, 1941.

According to the author this is the youngest case of omental cyst on record. It occurred in a 3 weeks' old female infant causing ileus with gangrene of the bowel terminating in death. The cyst measured 4 by 5 cm. and was composed of 2 layers. It was probably lymphogenous in origin.

FRANK SPIELMAN.

Pregnancy: Complications

Hull, Edgar: Tuberculosis and Pregnancy, New Orleans M. & S. J. **96:** 321, 1944.

It is estimated that active tuberculosis is present in 0.7 per cent of pregnant women. There are 32,000 pregnancies in this country each year complicated by this disease. However, the author feels that pregnancy has little effect upon the course of tuberculosis. Since the disease has its highest mortality during the most reproductive years, it stands to reason that many deaths will occur either during or just after a pregnancy. There is much evidence to support the thought that tuberculosis is neither affected favorably or unfavorably by pregnancy. The prognosis depends upon the stage of the disease and its treatment regardless of the pregnancy. The above conclusions are based upon the opinions of other quoted authors

and the study of 29 pregnant women with active tuberculosis. Of this group one woman died, 28 were presumably healthy following delivery and there were delivered to these women during the years of this study 34 healthy children. It may be concluded that pregnancy has little effect upon the course of the disease. The mortality rate in pregnant or recently pregnant women due to tuberculosis is not greater than nonpregnant women of similar ages. No patient has been aborted for active tuberculosis during the last 9 years at the Louisiana State University Hospital.

WILLIAM BICKERS.

Schenck, S. B., and Rader, M. J.: Spontaneous Rupture of Uterus in Fourth Month of Pregnancy, Am. J. Surg. **52:** 494, 1941.

This is a report of a case of spontaneous rupture of the uterus in the fourth month of pregnancy. The rupture occurred in the region of the right cornu at the site of a salpingectomy performed 16 months previously. It is also an example of transperitoneal migration of the ovum, since the corpus luteum was found in the right ovary.

FRANK SPIELMAN.

Cohen, Raymond C.: Effect of Pregnancy and Parturition on Pulmonary Tuberculosis, Brit. M. J. **4328:** 75, December 18, 1943.

Certain deductions are made from a study of 100 cases of pulmonary tuberculosis complicated by pregnancy. These are all sanatorium cases. It was found that pregnancy and labor per se, rarely exert any harmful effect on the progress of a woman known to have suffered from pulmonary tuberculosis and therapeutic abortion need not be resorted to. Active pulmonary disease is seldom accelerated by pregnancy and labor, and with treatment under favorable conditions, pregnancy has been little more than an incident in their tuberculous career. Careful consideration is given to the fact that these cases are all sanatorium patients, and the added discomforts of a life outside of a sanatorium which may precipitate a breakdown are absent. With proper care and treatment, the tuberculous woman may be allowed to proceed safely to term.

WILLIAM BERMAN.

Cohen, R. R.: Congenital Malaria, Obst. y ginec. Latino-Am. **1:** 431-436, 1943.

From an extensive experience in malaria district, the author comes to the conclusion that congenital malaria is a reality. He observed that mothers with plasmodium in the peripheral blood, bear children who had plasmodium in their peripheral blood, in the placenta and in the umbilical cord. Some of the newborn babies have fever and others die shortly after birth.

The author failed to find evidence of injury in any of the placentas of malarial babies and therefore he maintains that the passage of plasmodium takes place in healthy placentas. He prescribes euquinine during pregnancy in women who have malaria. This does not lead to abortion but on the contrary helps to prevent abortion which malaria has a great tendency to produce. In cases of toxemia, quinine must be used with great caution because of its tendency to produce hemolysis.

J. P. GREENHILL.

Sterility, Fertility, Contraceptives

Birnberg, C. H., Kurzrok, L., and Weber, H.: Effect of Pregneninolone (Ethinyl Testosterone) Upon Human Cervical Secretion, Am. J. Surg. **57:** 180, 1942.

Pregneninolone (pranone) was given to 6 patients all of whom manifested a negative semen penetration test, and 5 of whom showed an acid cervical secretion

(hydrogen ion concentration from 5 to 6). Following the administration of the material, the secretion became alkaline and the semen penetration test positive in 5 of the cases. Three subsequently became pregnant. One case was unchanged. The pregneninolone was administered in 10 mg. doses twice daily.

The semen penetration test consists in putting one drop of semen and cervical mucus upon a slide so that the surfaces become contiguous when covered by a glass cover slip. The test is positive if columns of spermatozoa can be seen microscopically in the cervical mucus. The test is negative when the spermatozoa are repelled by the mucus so that they cannot penetrate it.

FRANK SPIELMAN.

Murroy, E. G.: Gonadal Stimulation by Ascorbic Acid, Bol. Soc. de obst. y ginec. Latino-Am. **1:** 437-451, 1943.

In 18 cases of deficient spermatogenesis, the author prescribed ascorbic acid. The increase in the motility and viability of the spermatozoa and the decrease in the number of abnormal forms, led the author to recommend this therapy.

J. P. GREENHILL.

Sharman, Albert: Some Recent Studies and Investigations in Sterility, Proc. Roy. Soc. Med. **37:** 67, 1943.

The author reviews four aspects of the problem which he has investigated, namely, (1) on the estimation of tubal patency; (2) on anovular menstruation as assessed by endometrial biopsy; (3) on endometrial tuberculosis; and, (4) on the causation of tubal occlusion. He concluded that an isolated or occasional finding of apparent nonpatency may occur, and this, equally in anesthetized and nonanesthetized subjects, and the result of a single insufflation showing apparent nonpatency, cannot be depended upon. Among 115 patients who became pregnant, 29 had been diagnosed as having nonpatent tubes as a result of a single insufflation. The finding of nonpatency may occur at any time in the cycle. Tubal insufflation should be repeated several times before a diagnosis of nonpatency can be made.

It was found in this study that anovular menstruation is, therefore, a major infertility factor when it occurs, although the actual incidence is low. In reference to tuberculosis, it was found that although the incidence of the disease is minimal, endometrial tuberculosis is 15 times more common in sterile women than in those who are not. The authors feel that there is very little positive proof that, apart from gross tubal damage, gonococcal salpingitis is a common cause of tubal occlusion. The general condition appears to be that the gonococcus is seldom responsible for the occlusion of tubes which are not palpably thickened. Since the author found unsuspected subclinical endometrial tuberculosis in 5 per cent of sterile women, and since this is invariably secondary to tubal tuberculosis, it is highly probable that subclinical tubal tuberculosis is present in at least 5 per cent of sterile women. This is offered as an explanation for tubal blockage.

WILLIAM BERMAN.

Society Transactions

CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF OCTOBER 15, 1943

SYMPOSIUM ON CAUDAL ANESTHESIA

The following papers were presented:

Analgesia and Anesthesia for Obstetrics Inhalation Methods. W. Allen Conroy, Captain, M. C., A. U. S. (For original article, see page 81.)

Local Anesthesia. Henry Buxbaum, M.D. (For original article, see page 90.)

Continuous Caudal Anesthesia With Pontocaine: Obstetrician's Viewpoint. James E. Fitzgerald, M.D., James M. Thomson, M.D., and Hugh O. Brown, M.D. (For original article, see page 94.)

Continuous Caudal Anesthesia With Procaine Hydrochloride in 240 Obstetric Patients. William F. Mengert, M.D. (For original article, see page 100.)

PHILADELPHIA OBSTETRICAL SOCIETY

MEETING OF MARCH 2, 1944

The following papers were presented:

Myelogenous Leucemia Complicating Pregnancy. Helen M. Angelucci, M.D. (For original article, see page 125.)

Cesarean Section Morbidity and Septic Mortality in Relation to the Type of Operation. Clarence C. Briscoe, M.D. (For original article, see page 16.)

The Prognosis and Management of Premature Rupture of the Membranes. Edward H. Bishop, M.D. (For original article, see page 45.)

Item

Directory of Medical Specialists

The third edition of the Directory of Medical Specialists listing names and biographic data of all men certified by the fifteen American Boards is to be published early in 1945. Collection of biographic data of the Diplomates certified since the 1942 edition, and revision of the older listings in that volume are now going forward rapidly. Diplomates are requested to make prompt return of notices regarding their biographies as soon as possible after receiving the proper forms from the publication office soon to be mailed to them.

Erratum

Dosage of Ethinyl Estradiol

In the article by Robert A. Lyon, entitled "Management of the Climacteric With Ethinyl Estradiol," published in the April, 1944 issue, page 534, the sentence, "attempts to decrease the dosage to 20, 30 or 40 milligrams of ethinyl estradiol daily resulted in the reappearance of flashes in most patients who had been controlled with 50 milligrams," should read as follows:

> *"attempts to decrease the dosage to 0.02, 0.03, or 0.04 mg. of ethinyl estradiol resulted in the reappearance of flashes in most patients who had been controlled with 0.05 mg."*

ROSTER OF AMERICAN OBSTETRICAL AND GYNECOLOGICAL SOCIETIES*

(Appears in January, April, July, October)

American Gynecological Society. (1876) *President,* Edward A. Schumann, Philadelphia, Pa. *Secretary,* Howard C. Taylor, Jr. 842 Park Ave., New York, N. Y. Next annual meeting, June, 1945.

American Association of Obstetricians, Gynecologists and Abdominal Surgeons. (1888) *President,* W. R. Cooke, Galveston, Texas. *Secretary,* James R. Bloss, 418-11th Street, Huntington, W. Va. Annual meeting Hot Springs, Va., Sept. 1944.

Central Association of Obstetricians and Gynecologists. (1929) *President,* John H. Moore, Grand Forks, N. D. *Secretary-Treasurer,* W. F. Mengert, Dallas, Tex. Annual meeting not announced.

South Atlantic Association of Obstetricians and Gynecologists. (1938) *President* Oren Moore, Charlotte, N. C. *Secretary,* T. J. Williams, University, Va. Annual meeting cancelled.

A. M. A. Section on Obstetrics and Gynecology. *Chairman,* Philip F. Williams, Philadelphia, Pa. *Secretary,* William Mengert, 2211 Oak Lawn Ave., Dallax Tex. Next meeting, New York City, June, 1945.

New York Obstetrical Society. (1863) *President,* W. E. Studdiford. *Secretary,* R. G. Douglas, 530 East 70th St., New York City. Second Tuesday, from October to May, Yale Club.

Obstetrical Society of Philadelphia. (1868) *President,* Charles A. Behney *Secretary,* John B. Montgomery, Pro tem, 1930 Chestnut St., Philadelphia, Pa. First Thursday, from October to May.

Chicago Gynecological Society. (1878) *President,* William J. Dieckman. *Secretary,* Herbert E. Schmitz, 25 East Washington Ave., Chicago, Ill. Third Friday, from October to June, Hotel Knickerbocker.

Brooklyn Gynecological Society. (1890) *President,* James P. McManus. *Secretary,* William T. Daily, 142 Joralemon St., Brooklyn, N. Y. First Friday, from October to May, Kings County Medical Society, 1313 Bedford Ave., Brooklyn, N. Y.

Baltimore Obstetrical and Gynecological Society. (1929) *President,* Lawrence Wharton. *Secretary-Treasurer,* John W. Haws, 9 E. Chase St., Baltimore, Md. Meets quarterly at Maryland Chirurgical Faculty Bldg.

Cincinnati Obstetrical Society. *President,* Edward Friedman. *Secretary,* Carroll J. Fairo, Cincinnati, Ohio. Third Thursday of each month.

Louisville Obstetrical and Gynecological Society. *President,* Layman A. Gray. *Secretary,* E. P. Solomon, Hegburn Bldg., Louisville, Ky. Fourth Monday, from September to May, Brown Hotel.

Portland Society of Obstetrics and Gynecology. *President,* Howard Stearns. *Secretary,* William M. Wilson, 545 Medical Arts Bldg., Portland, Ore. Last Wednesday of each month.

Pittsburgh Obstetrical and Gynecological Society. (1934) *President,* David B. Ludwig. *Secretary,* Joseph A. Hepp, 121 University Place, Pittsburgh, Pa. First Monday of October, December, February, April, and June.

Obstetrical Society of Boston. (1861) *President,* Thos. Almy, Fall River, Mass. *Secretary,* Paul A. Younge, 101 Bay State Road, Boston, Mass. Third Tuesday, October to April, Harvard Club.

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*Changes, omissions, and corrections should be addressed to the Editor of the JOURNAL. The number after the name is the year of founding.

New England Obstetrical and Gynecological Society. (1929) *President,* Frank A. Pemberton. *Secretary,* Fred. J. Lynch, 475 Commonwealth Ave., Boston, Mass. Meetings held in May and December.

Pacific Coast Obstetrical and Gynecological Society. (1931) *President,* T. Floyd Bell. *Secretary-Treasurer,* William Benbow Thompson, 6253 Hollywood Blvd., Los Angeles, Calif.

Washington Gynecological Society. (1933) *President,* James R. Costello. *Secretary,* J. Keith Cromer, 1835 Eye St., N.W., Washington, D. C. Fourth Saturday, October to May.

New Orleans Obstetrical and Gynecological Society. (1924) *President,* E. L. Zander. *Secretary,* R. A. Grasser, 2700 Napoleon Ave., New Orleans, La. Meetings held every other month.

St. Louis Gynecological Society. (1924) *President,* S. A. Weintraub. *Secretary,* Joseph A. Hardy, Jr., 4952 Maryland Ave., St. Louis, Mo. Meetings second Thursday, October, December, February, and April.

San Francisco Gynecological Society. (1929) *President,* R. Glenn Craig. *Secretary,* D. G. Morton, California University Hospital, San Francisco, Calif. Regular meetings held second Friday in month from October to April, University Club, San Francisco, or Claremont Country Club, Oakland, Calif.

Texas Association of Obstetricians and Gynecologists. (1930) *President,* T. F. Bunkley. *Secretary,* J. McIver, 714 Medical Arts Bldg., Dallas, Tex.

Michigan Society of Obstetricians and Gynecologists. (1924) (Formerly the Detroit Obstetrical and Gynecological Society.) *President,* Norman F. Miller. *Secretary,* Milo R. White, 2799 W. Grand Blvd., Detroit, Mich. Meetings first Tuesday of each month from October to May (inclusive).

Obstetric Society of Syracuse Hospitals. (1938) *President,* Edward C. Hughes. *Secretary,* Nathan N. Cohen, 713 E. Genesee St., Syracuse, N. Y. Meets second Tuesday of September, November, January, March, and May. Suspended for the duration.

Alabama Association of Obstetricians and Gynecologists. *President,* J. M. Weldon, Mobile, Ala. *Secretary,* Eva F. Dodge, Montgomery, Ala.

San Antonio Obstetric Society. *President,* I. T. Cutter. *Secretary,* S. Foster Moore, Jr., San Antonio, Tex. Meetings held first Tuesday of each month at Gunter Hotel.

Seattle Gynecological Society. (1941) *President,* R. Philip Smith. *Secretary,* Gerhard Ahnquist, 1336 Madison Street, Seattle. Meetings third Wednesday.

Denver Obstetrical and Gynecological Society. (1942) *Secretary,* Emmett A. Mechler, 1612 Tremont St., Denver, Colo. Suspended during war.

Wisconsin Society of Obstetrics and Gynecology. (1940) *President,* Roland S. Cron. *Secretary,* Robert E. McDonald, 425 E. Wisconsin Ave., Milwaukee, Wis. Meetings held in May and October.

San Diego Gynecological Society. (1937) *President,* Geo. D. Huff. *Secretary,* Frank Russell, 233 A St., San Diego, Calif. Meetings held on the last Wednesday of each month.

North Dakota Society of Obstetrics and Gynecology. (1938) *President,* John D. Graham, Devil's Lake. *Secretary,* G. Wilson Hunter, 807 Broadway, Fargo, N. D.

Virginia Obstetrical and Gynecological Society. (1936) *President,* A. L. Carson, Jr. *Secretary,* L. L. Schamburger, 628 State Office Bldg., Richmond, Va. Next meeting not announced.